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VENOGRAPHY IN THE DIAGNOSIS OF PELVIC TUMOURS

by

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The determination of the presence as well as the nature and spread of an expanding lesion in the bony pelvis presents clinical and roentgenologic difficulties emphasizing the need for improved diagnostic methods. Since both primary tumours and metastases from malignant tumours are situated close to blood vessels, angiography would seem to be the method of choice. Arteriography may in certain cases afford information concerning the position and sometimes also the nature of an expanding lesion by demonstrating the displacement of vessels or the presence of tumour vessels. The blood pressure in veins is low and the walls are thin; in consequence, expanding lesions close to these vessels may cause indentations or complete occlusion. Furthermore, the contrast medium may, by reason of the change in the intravenous pressure, pass through anastomoses not normally filled.

Different roentgenologic means of showing the pelvic veins have been described. The selective injection of contrast medium through the marrow of the pelvic bones has been used by many authors (5, 6, 15, 16, 3, 18, et al.). De la Pena, Baux & Poulhes, and Petkovic, inter alios, have injected contrast medium into the deep dorsal vein of the

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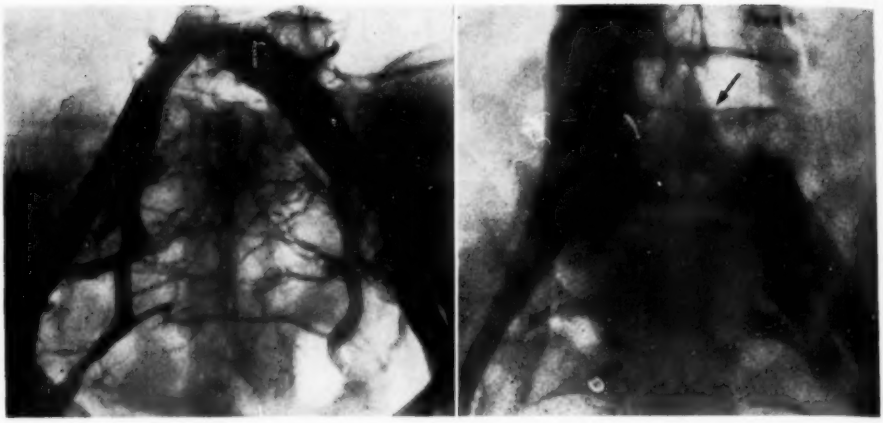

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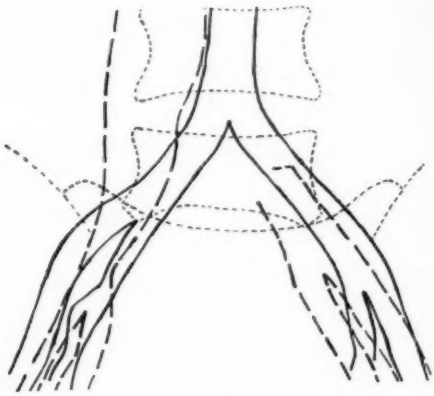

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Fig. 1. Normal cases. a) After compression of distal part of inferior vena cava, pelvic veins well filled. b) Venography: Defect in left common iliac vein (←). c) Schematic illustration of venographic (— —) and arteriographic (———) films, both exposed in the same projection. Defect in left common iliac vein caused by compression of vessel between spinal column and both common iliac arteries.

penis or clitoris. These methods are painful and complications such as pulmonary embolism and local haemorrhages have been reported (15, 10). GANSAU has obtained retrograde filling of the pelvic veins by direct injection into the inferior vena cava. According to many authors the method of examination best tolerated by the patient is the injection of contrast medium into the femoral vein, either percutaneously or after it has been surgically exposed. Only the external and common iliac veins and the inferior vena cava get filled unless a constriction or occlusion is present in any of these veins. As no, or but incomplete contrast filling of the internal iliac vein and its branches occurs, this kind of examination has

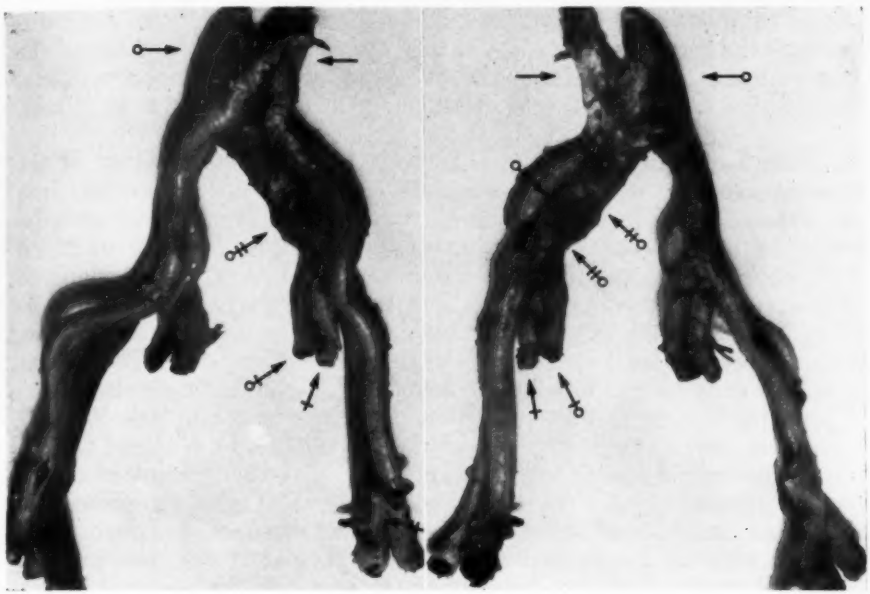

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Fig. 2. Autopsy specimen. Normal case. Vessels filled with plastic solution before dissection. a) A. p. and b) p. a. projection. Aortic bifurcation (←). Inferior vena cava (←○). The anatomic relations between the internal iliac vein (↔○), internal iliac artery (↔), and external iliac vein, as well as between the inferior epigastric artery (↔) and external iliac vein are seen. Corresponding to the promontorium there is a cone-shaped indentation in left common iliac vein from behind producing an increased lateral diameter (↔○). The indentation is most marked on the medial side.

been of only limited value in investigating and diagnosing expanding lesions in the pelvis.

Fariñas, Helander and Lindbom, inter alios, have demonstrated the possibility of obtaining retrograde filling of the pelvic veins by compression of the distal part of the inferior vena cava. This modification increases the value of the method in demonstrating pathologic changes in or near the pelvic veins. The value of pelvic venography in the diagnosis of tumours has been pointed out by several authors (6, 1, 8, 16, 10, 13), although no account of the changes and their diagnostic value appears to have been published. Our material is fairly small, but mostly comprises verified cases and it may therefore be of interest to give a report of our experiences based on the verified cases, negative as well as positive.

Technique

Examination of the pelvic veins has been performed in our department since the end of 1955. During the first few months retrograde contrast filling of the internal iliac vein and its branches was obtained by

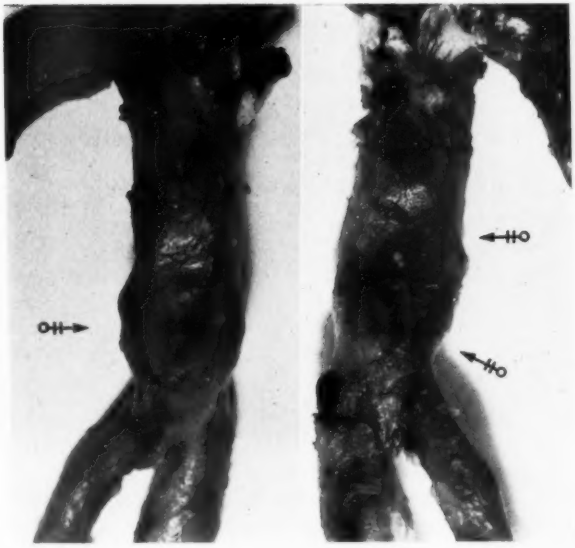
forced expiration. The filling was, however, often incomplete. After discussing the problem with HELANDER and LINDBOM, who stressed the importance of compression of the distal part of the inferior vena cava, we changed our method (Fig. 1 a). Our present technique is as follows.

After local anaesthesia and bilateral percutaneous puncture of the femoral vein in the groins, polyethylene catheters are introduced into the external iliac veins. The introduction of catheters is not essential but is an easy procedure and simplifies the examination. About 20 ml 20 % contrast medium (of the 3-iodised water-soluble type, now commonly used) is injected simultaneously into both catheters as quickly as possible. The examination is carried out in two stages, first without, then with compression of the distal part of the inferior vena cava. The patient is usually examined supine, but occasionally oblique views are also taken. When compression is not applied, contrast filling is usually not obtained peripheral to the tip of the catheter. In order to fill as much of the external iliac vein as possible, the tip of the catheter is introduced only a few centimeters into the vessel. An examination without compression is performed in order to study the blood circulation and particularly to find out whether a collateral circulation is present or not. Compression is applied by means of the same apparatus as we use for urography, with the rubber balloon against the lower part of the abdomen at the level of the iliac crests and somewhat to the right of the midline.

An automatic film cassette changer is employed; this is not essential but in some cases rapid film changing is necessary to show the direction of the blood flow in the collaterals. The first film is exposed as, or immediately after the injection is started. During the examination without compression about four films are exposed at intervals of 1 sec. Following the application of compression, when the rate of the local circulation is decreased, 6 to 8 films are exposed at 2 sec intervals.

The examination is easy to perform and the contrast injection causes no more discomfort to the patient than an ordinary injection in urography. No complications have been observed which could be ascribed with certainty to the examination but in two cases autopsy revealed thrombotic material bilaterally in the femoral and external iliac veins and pulmonary embolism. These cases are briefly reported below.

A man, 72 years (Case 14), suffering from schizophrenia and cancer of the urinary bladder, with metastases (the size of a mandarin) in the pelvis in front of the sacrum, as well as in the lymph nodes along the left external iliac vein. His general condition on admission was poor, and he lay very still in bed. He deteriorated progressively and died 25 days after the venography. No operation was performed and the patient received no anti-



a b

Fig. 3. Same specimen as in fig. 2, showing details of left common iliac vein, (a) in a. p., and (b) in p. a. projection.

thrombotic treatment. Post-mortem examination revealed thrombotic material adherent to the walls of the femoral and iliac veins on both sides, as well as small pulmonary emboli.

A woman, 66 years (Case 13), operated on one year previously for cancer of the rectum with metastases in the lymph nodes, was readmitted with palpable lymph node metastases in the left groin. At pelvic venography, expanding lesions were found along the common iliac veins and the left external iliac vein. Furthermore, there was displacement of the right internal iliac vein, and compression did not result in retrograde filling of the left internal iliac vein. The patient was operated upon and found to have lymph node metastases along the vessels as shown earlier by venography. Irregular cystic metastases (the size of a child's head) were discovered in the right ovary and spreading into the pelvic wall on the left side. Biopsy was performed upon the ovarian tumour. The post-operative condition was satisfactory until the patient died suddenly of pulmonary embolism, 14 days after venography and 12 days after operation.

In neither of these cases can it be proved that the vein puncture or catheterization caused the thrombosis, but on the other hand this possibility is difficult to eliminate. In the first case, the tumour with metastases together with the lack of active movement by the patient may in themselves have been responsible for the thrombosis. In the second case the thrombosis may be explained by the primary tumour with metastases surrounding the vessels, together with manipulations during operation. No other complications have been observed.

Material and results

Forty-four examinations have been performed in 39 cases of suspected pelvic tumours. The changes observed in the veins in 30 verified cases were: displacement, indentation and incomplete filling of the veins (in the direction of the blood flow or contra-wise), decreased rate of flow in various parts of the venous system, presence of dilated veins, and contrast filling of anastomoses. In order to find out whether such changes may occur in the absence of an expanding lesion, those films in which subsequent operation revealed no pelvic tumour were reexamined.

Normal cases

In the 9 normal cases two different types of changes have been observed, viz. indentations and contrast filling of anastomoses without compression of the inferior vena cava.

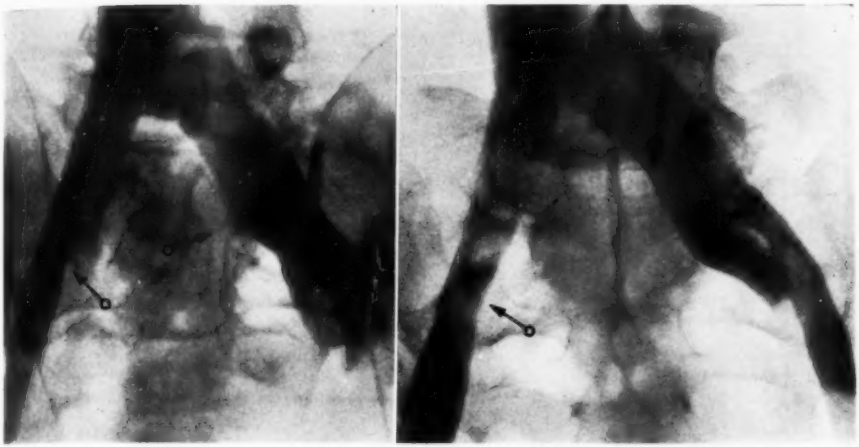
Indentations were observed in the left common iliac vein just before its opening into the vena cava, in the external or common iliac veins at the level of the pelvic inlet, in the external iliac vein at its junction with the internal iliac vein, and on the lateral aspect of the external iliac vein close to the inguinal ligament.

HELANDER and LINDBOM believe that indentations in the left common iliac vein are caused by its compression between the vertebral column and the aortic bifurcation. We have been able to verify this in cases in which aortograms and corresponding venograms were compared (Fig. 1, b and c).

In order to investigate other types of indentations of the veins in normal cases, post-mortem examinations of the pelvic vessels were performed in subjects without expanding lesions in the pelvis. — A special technique was employed. A fluid plastic substance was injected into the pelvic arteries and veins from the aorta and into the inferior vena cava. The vessels maintained their shape after the injected fluid had set and were then dissected and examined. This examination which was carried out by HANS ECKERBOM is gratefully acknowledged.

Indentations in the veins at the level of the pelvic inlet were shown to be caused by their compression against the promontorium (Figs. 2, 3 and 4 a). The diameter of the involved vein is consequently increased in the lateral and decreased in the sagittal direction. This gives an impression of a slight indentation in the vein just above and below the promontorium; the change is most marked on the medial aspect of the vein.

Indentations in the external iliac vein just before it joins the internal iliac vein, may be caused in at least two different ways. The internal



a b

Fig. 4. Venography in 2 normal cases. a) A change, similar to the one in figs. 2 and 3 is seen (⟷) in left common iliac vein. In both a) and b) a small indentation of somewhat different appearance in right external iliac vein just below its junction with internal iliac vein (⟵). The latter change may be due to the internal iliac artery.

iliac artery in this region runs medially and close to the external iliac vein, in the angle between this vessel and the internal iliac vein. Hence the artery may cause a slight indentation in the medial aspect of the external iliac vein (Figs. 2 and 4). If the internal vein is not filled in a retrograde direction the blood flow from this vein may cause a dilution of the contrast medium and produce a false impression of an indentation at its termination.

Indentations on the lateral aspects of both external iliac veins at the level of the inguinal ligaments were observed in one case before the application of compression of the vena cava (Fig. 5 upper view). This change disappeared when the compression was applied (Fig. 5 lower view) and consequently could not be caused by any rigid fixed tissue, as for instance, in the walls of the lacuna vasorum. Enlarged lymph nodes are commonly present in the groins and may produce indentations similar to those already mentioned. Since the changes present in our case were symmetrical there was possibly some other anatomical cause. The inferior epigastric artery arises from the medial aspect of the femoral artery or external iliac artery, at the level of the inguinal ligament and runs close enough to the vein to cause an indentation (Cf. Fig. 2).

A thin contrast filling of the ascending lumbar vein on one or both sides may occur without compression of the inferior vena cava. This has

Table

Case	Sex and age	Diagnosis	Changes observed					
			Displacement	Indentation	Non-filling of part of veins	Contrast-filled anastomoses	Widening	Slow drainage
1	♀ 60	Fibrosarcoma lig.lat. uteri dx. ...	+	—	+	—	—	—
2	♀ 37	Salpingo-oophorit. chron. sin.	+	+	+	—	—	—
3	♀ 44	Cancer ovarii sin.	+	+	—	—	—	—
4	♀ 55	Cancer ovarii bilat.	+	+	+	+	+	—
5	♀ 45	Cancer uteri c. metast.	+	+	—	+	—	—
6	♀ 59	» » » »	—	+	—	+	—	—
7	♀ 56	» » » »	—	+	—	—	—	—
8	♀ 56	Cancer ovarii sin. op. c. metast.	—	—	+	—	+	—
9	♀ 59	» » » » » »	—	+	—	+	—	+
10	♂ 59	Cancer coli op. c. metast.	+	+	—	—	—	—
11	♀ 51	» » » » »	—	+	+	+	—	—
12	♀ 31	Cancer recti op. c. metast.	—	+	+	+	—	+
13	♀ 66	» » » »	+	+	+	—	—	—
14	♂ 72	Cancer ves. urinar. c. metast.	+	+	—	—	—	—
15	♂ 65	Hodgkin's disease	—	+	+	+	—	—
16	♀ 68	Leukemia myel. chron.	—	+	—	—	—	—
17	♀ 37	Cancer uteri op. + Periphlebit. ..	—	—	+	+	+	—
			8	14	9	8	3	2

most often been observed on the left side, perhaps due to a slight compression of the left common iliac vein between the spine and the aorta. The ascending lumbar vein is narrow.

Faint and incomplete contrast filling of the internal iliac vein and some of its branches may also occur in a retrograde direction without simultaneous compression of the inferior vena cava, or during Valsalva's manoeuvre performed by the patient. In this material there has been either no filling or bilateral filling of these veins.

No other changes have been observed in the normal cases.

Cases with expanding lesions

Twenty-one cases with verified expanding lesions have been studied, 6 of which were verified by autopsy and 14 by operation. In one (Case 15), the verification was not quite definite. The case was one of Hodgkin's disease, histologically verified, and the changes shown by contrast injection of the pelvic veins and the vena cava decreased considerably after roentgen treatment. In all cases, verification of the diagnosis was obtained shortly after the venography.

In 17 out of the 21 cases (See Table) definite changes could be demonstrated. In the remaining 4 cases no obvious changes were visible; in these the examination was incomplete inasmuch as compression of the

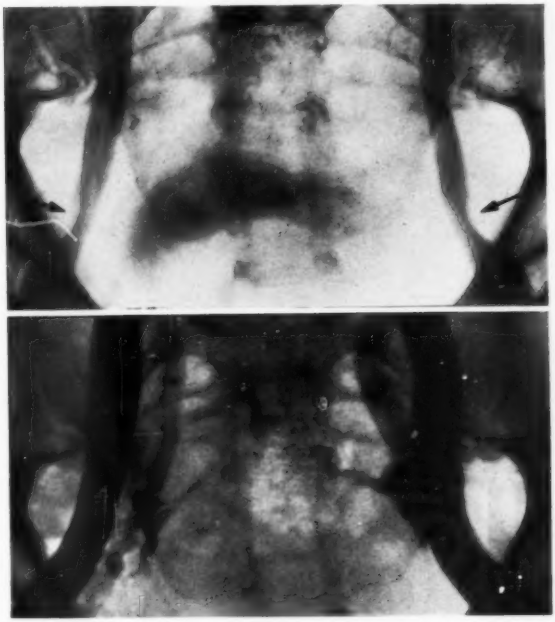
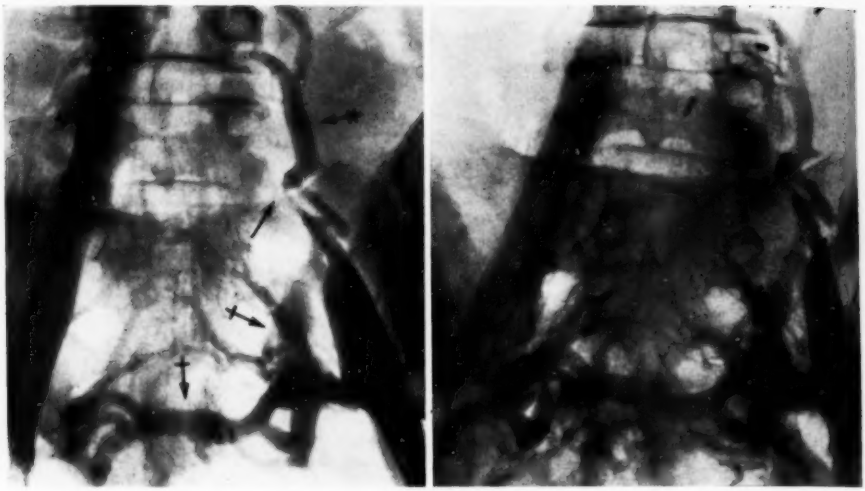


Fig. 5. Normal case. *Upper* view before, and *lower* after compression of inferior vena cava. Lateral symmetric indentations in both external iliac veins at level of inguinal ligament (←). These completely disappear after compression of vena cava and may be caused by the inferior epigastric artery. (Cf. fig. 2 a).

inferior vena cava was not applied, or was ineffective, and the internal iliac vein and its branches could consequently not be studied.

The changes most often observed were indentations of the pelvic veins which occurred in 14 cases. The change second in frequency was non-filling of a part of the veins. This was noted in 9 cases, in 3 of which the contrast filling was deficient in the direction of the blood flow, and in the remaining 6 normal retrograde filling was absent in part of the venous system. The first change is certainly pathologic and caused by occlusion. The evaluation of the other change is more doubtful since retrograde filling may normally be different on both sides, even though this was not observed in our normal cases. If a deficient retrograde filling of a part of the pelvic veins is the only abnormality observed, this may be an indication to inject more contrast medium peripherally to the suspected occlusion, *e. g.* into the marrow of the pelvic bones.

Displacement of veins was observed in 8 cases. Displacement is difficult to estimate particularly as regards small veins, and a detailed knowledge of the anatomic variations in normal veins is essential.



a b

Fig. 6. Changes caused by metastases in lymph node and left ovary from rectal carcinoma. a) Before and b) after operation; metasasis indicated by metal clips. No compression of vena cava. Total occlusion of left common iliac vein (←). The contrast medium passed through the slightly widened internal iliac vein and its branches (↔) and through the somewhat widened ascending lumbar vein (↔).

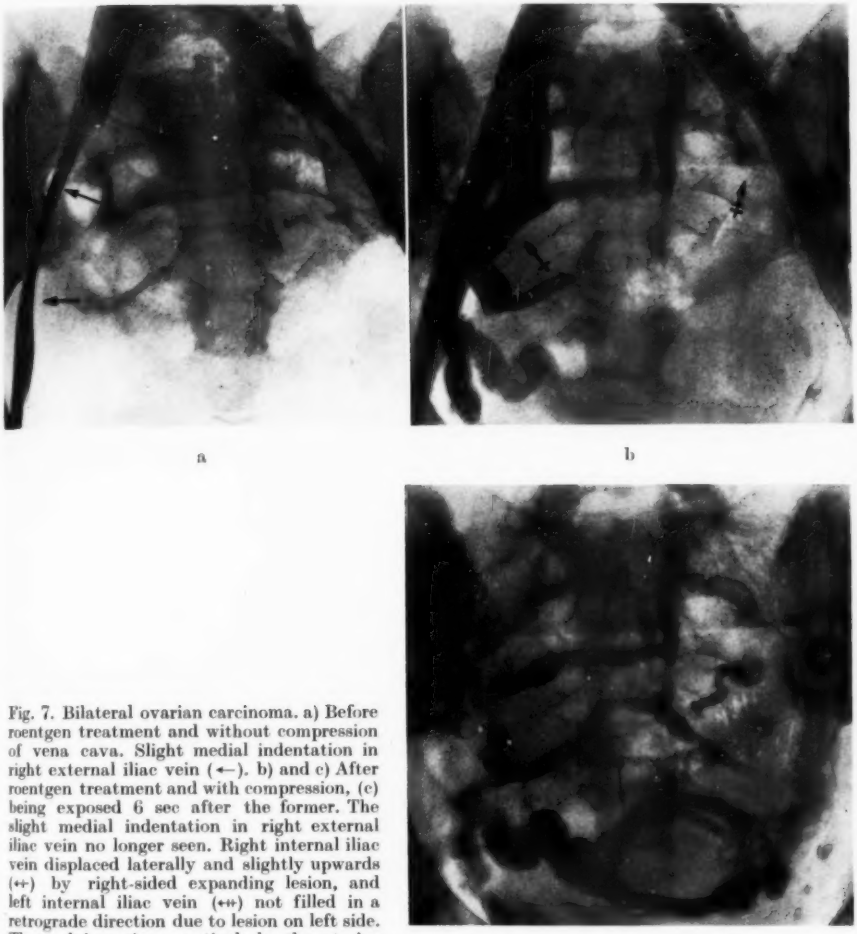
Contrast filling of anastomoses was also observed in 8 cases. Pathologic collateral circulation with contrast filling of the anastomotic vessels occurs with an increase in venous pressure. Such an increase in pressure may occur with cardiac insuffiency and occlusion in the inferior vena cava, in which case the filling of the anastomosis is probably symmetrical. Unilateral anastomotic filling in the pelvis, shown by rapid serial films, is caused by occlusion in the pelvic veins.

Some of the pelvic veins may become wider following the increase in the blood flow, as was shown in 3 of our cases.

Slow drainage of a part of the venous system occurred in 2 cases. Contrast medium remained in the small peripheral branches of the internal iliac vein several seconds after it had disappeared from the larger branches of the vessels. In both cases, an expanding lesion was present in the pelvis, possibly causing compression of the veins in the periphery of that area, where the contrast medium remained.

In all cases, except 2 (Cases 7 and 16) several types of changes were observed.

The value of pelvic venography is apparent from the following case reports.

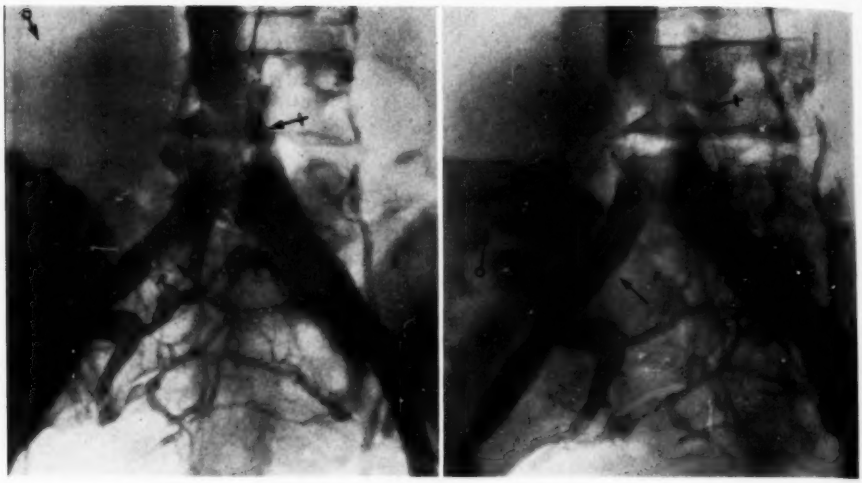


a b c

Fig. 7. Bilateral ovarian carcinoma. a) Before roentgen treatment and without compression of vena cava. Slight medial indentation in right external iliac vein (←). b) and c) After roentgen treatment and with compression, (c) being exposed 6 sec after the former. The slight medial indentation in right external iliac vein no longer seen. Right internal iliac vein displaced laterally and slightly upwards (↔) by right-sided expanding lesion, and left internal iliac vein (↔) not filled in a retrograde direction due to lesion on left side. The pelvic veins, particularly the uterine vessels (←○) widened.

A woman, 31 years (Case 12), operated upon 4 years previously for cancer of the rectum, had been suffering for a year from severe pain in the region of the left femoral cutaneous nerve. Roentgen examinations of the pelvis and lumbar spine were normal. Urography was not carried out.

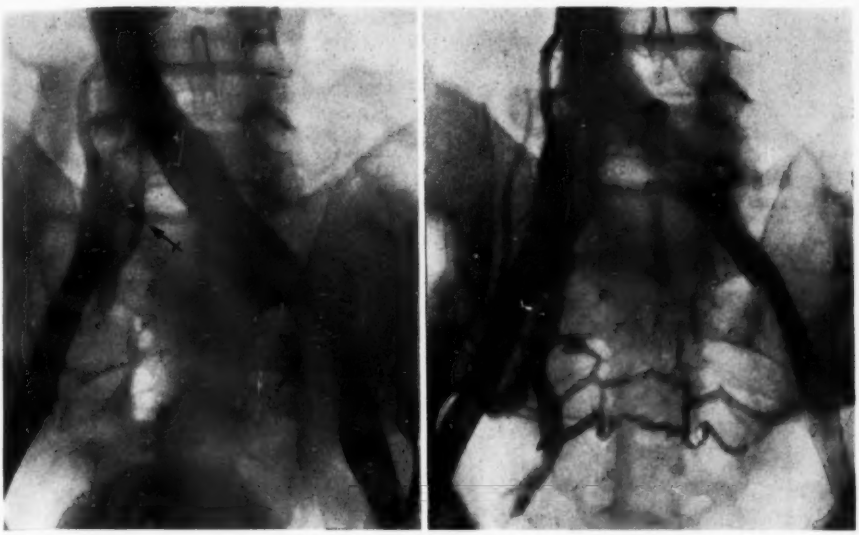
Pelvic venography (Fig. 6 a) was performed without compression of the inferior vena cava. The left common iliac vein was occluded and distal to the block an irregular indentation was seen. Contrast medium injected into the left external iliac vein passed through the somewhat widened internal iliac vein and its branches and the similarly widened ascending lumbar vein.



a b

c

Fig. 8. Uterine cancer with metastases. No compression of vena cava. a) A. p. b) and c) Oblique. Indentation in medial aspect of right common iliac vein (←) and a larger indentation in distal part of inferior vena cava (↔) The latter change is not caused by bony proliferations of L 4 and L 5 (c). Soft tissue mass at the level of L 4—L 5 (←○). Due to obstruction to blood flow in vena cava, pelvic veins are filled without compression.



a b

Fig. 9. Hodgkin's disease. a) Before roentgen treatment, without compression or straining. Large indentation in left external iliac vein (+–) and right common iliac vein (++). b) After treatment, with straining. Indentation in left external iliac vein is smaller but there is no retrograde filling of left internal iliac vein, indicating that a tumour is still present. Appearances of right common iliac vein unchanged.

Operation revealed a metastasis (about 3 × 3 cm) at the site of the occlusion and another metastasis, not quite so large, in the left ovary, situated close to the left side of the sacrum.

Biopsy from the metastases showed adenocarcinoma of the same type as in the primary tumour. The tumours could not be extirpated but were marked with silver clips (Fig. 6 b) and a course of intense roentgen treatment was given. The subsequent course was uneventful and the patient is still completely free from symptoms 18 months after examination; she has increased in weight and feels well.

A woman, aged 55 years (Case 4), with bilateral ovarian carcinoma; a tumour the size of a clenched fist was palpable on the right side, and one the size of a goose's egg on the left.

Pelvic venography was performed twice preoperatively, once before and once after roentgen treatment. The first examination (Fig. 7 a) was performed without compression of the inferior vena cava and without straining by the patient. This showed an extended indentation in the medial aspect of the right external iliac vein.

Urography following the venography revealed a moderate degree of hydro-ureter and hydronephrosis on the right side.

The second venography (Figs. 7 b, 7 c) was performed 2 months later and a few days before operation; on this occasion compression was applied to the inferior vena cava. No obvious indentation in the right external iliac vein was observed, but the first and second examinations are not quite comparable since different methods were employed. The right

internal iliac vein was displaced laterally and somewhat upwards in its lower part. The left internal iliac vein did not fill in a retrograde direction but the widened pelvic veins were filled from the right side.

Urography following this venography demonstrated that the right-sided hydroureter and hydronephrosis, previously observed, had almost disappeared.

Operation disclosed growths of the ovaries, the tumours being reduced to the size of hen's eggs; no metastases could be seen. The patient died two months after operation; autopsy revealed tumour infiltration in the pelvis, peritoneal carcinosis, and metastasis in the omentum.

A woman, aged 59 years (Case 6), who had received roentgen treatment for carcinoma of the uterus was admitted with a history of repeated attacks of pyelitis. Urography and retrograde pyelography revealed stenosis of the right ureter at the level of the L 4—L 5 joint and the pelvic inlet.

Pelvic venography (Fig. 8) was performed without compression of the inferior vena cava and without the patient straining. A small indentation was shown in the right common iliac vein, and a larger indentation (about 3 × 1 cm) in the distal part of the inferior vena cava. The last could not depend on the bony proliferations from the vertebral bodies, as shown in Fig. 8 c. Due to these indentations the pelvic and vertebral veins filled to a greater extent than normally. Moreover, there was a soft tissue mass, measuring about 3 × 3 cm, on the right side at the level of the L 4—L 5 joint. The indentations were situated at the level of the already observed ureterostenoses.

The changes described were fully explained at operation. The soft tissue mass was a necrotic metastasis and the indentation in the distal part of the vena cava was a lymph node metastasis spreading into the vein. There was a tumour growth on the right side at the level of the pelvic inlet.

A man, 65 years (Case 15), with histologically verified Hodgkin's disease. He was admitted on two occasions to the surgical clinic for atypical abdominal pain.

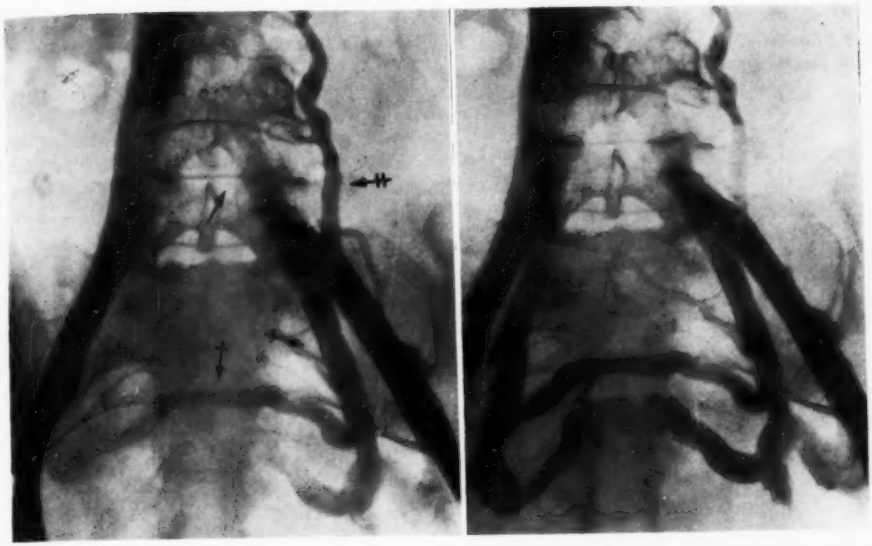
Venography and cavography were performed both before and after roentgen treatment. Compression was not applied on either occasion, but the second time the patient assisted by straining.

The first *venography* (Fig. 9 a) revealed a large indentation in the left external iliac vein and another of similar appearance in the right common iliac vein.

Following roentgen treatment the change in the right common iliac vein remained unaltered but the one in the left external iliac vein was considerably diminished (Fig. 9 b). The left internal iliac vein was not filled in a retrograde direction, in all probability due to the lymph node enlargement causing compression of the vein.

Cavography revealed expanding retroperitoneal lesions which decreased considerably after roentgen treatment.

Some of the changes in the pelvic veins occurring with expanding lesions may be found in other conditions such as thrombosis and periphlebitis. These lesions may cause obstruction to the venous drainage resulting in deficient contrast filling of a part of the local venous system, widening of the veins, and the development of a collateral circulation. On the other hand, displacement and true indentation should not occur in these two conditions, which may be of help in differentiating them from expanding lesions. The difficulty in the differential diagnosis is exemplified in the following case report.



a b

c

Fig. 10. Uterine cancer (operated). Periphlebitis of left common iliac vein. No metastases. No compression of vena cava. a) and b) A. p. views exposed at 2 sec intervals. c) Left side up. Cone-shaped occlusion of contrast medium in left common iliac vein (←) the medium passing from the left side, partly through the slightly widened internal iliac vein and its branches (↔), and partly through the widened left ascending lumbar vein (↔). Indentation from behind in distal part of inferior vena cava, caused by L 4 and L 5.

A woman, 37 years (Case 17), who had received a course of roentgen treatment for carcinoma of the uterine cervix in 1953. In 1955 she complained of pain in the right side of the abdomen.

Operation was performed with extirpation of the uterus, salpingo-oophorectomy, and bilateral removal of the pelvic lymph nodes. No metastases were found.

In 1956 following persistent symptoms, *pelvic venography* (Fig. 10) was performed without compression or Valsalva's manoeuvre. An occlusion in the left common iliac vein was shown. The contrast medium passed through the left internal iliac vein and its branches to the right internal iliac vein and through the widened left ascending lumbar vein. There were no displacements or indentations.

Urography showed no ureterostenosis.

At operation a moderate narrowing, 2 cm long, of the common iliac vein, corresponding to the change observed at venography, was found. The wall of the vein was a whitish colour and sclerotic, but there was no thrombosis. The change in the vein appeared similar to that described by WANKE and GUMRICH and was believed to be due to periphlebitis. No evidence of metastases.

On several occasions after puncture of the femoral veins, the venous pressure on the side involved seemed to be increased and the blood was often darker on that side than on the other. In order to study this in a more objective way, a recording was obtained of the venous pressure, oxygen saturation and lactic acid content of the blood, in co-operation with B. SÖDERHOLM of the clinical-physiologic department. This study was performed in ten cases in order to find out whether alterations in these data could be demonstrated even in cases with fairly small changes in the pelvic veins. If this were so the recording might prove of some help in doubtful cases, in determining whether changes in the veins were of pathological significance or not. In some cases alterations were revealed on the side involved, peripherally to the expanding lesion, *i. e.* somewhat increased venous pressure, diminished variations in the pressure with deep breathing and Valsalva's manoeuvre, decreased oxygen saturation, and increased lactic acid content. The alterations were, however, often small or insignificant in spite of obvious pathologic changes shown by pelvic venography. The recording of the venous pressure, oxygen saturation, and lactic acid content, thus appears to be of no essential diagnostic value, anyhow in cases in which sufficient collateral circulation has been established.

Conclusions

Venography can under suitable conditions reveal even comparatively small expanding lesions, even less than about 3 × 1 cm in size. In some of the cases reported, venography supplemented the clinical and roentgenologic methods and was of value in the localization of expanding lesions. In 4 cases, venography was the only method, apart from laparotomy, which could show the presence of metastases. In 5 other cases it is

doubtful if any other method of examination could have revealed the lesion.

As far as the nature of a lesion is concerned, venography alone is of little value, as both malignant and benign expanding lesions produce similar changes in the veins. When an expanding lesion is situated close to the ureter, ureterostenosis may occur; even a small malignant tumour or metastases may cause a stricture of the ureter by infiltration. A benign tumour, on the other hand, may cause displacement of the ureter, but no stenosis unless the mass is large enough to produce compression.

Thus urography is of greater help in determining the nature of expanding lesions. In our material, except in 1 case, ureterostenosis occurred only in cases of carcinoma and metastases. If urography is not performed earlier it is advisable to investigate renal excretion following the venography.

Pelvic venography is doubtless of considerable diagnostic value, but there may be a certain risk of thrombosis after the examination. It should therefore be performed only when clinical and other roentgenologic methods have failed to furnish sufficient information and the patient is physically well enough to be up and about afterwards. Prophylactic anticoagulant therapy may also be instituted after the examination, in which case any planned operation must be postponed.

SUMMARY

Pelvic venography was performed in 30 verified cases. Normal variations similar to those seen in pathologic cases are discussed on the bases of 9 verified negative cases. Pathologic changes in the form of displacement and indentation, with or without changes in the haemodynamics, were observed in 17 out of 21 positive verified cases. Venography is a valuable supplement to other methods in diagnosing expanding lesions in the bony pelvis and in some cases affords the only means of determining their presence. Urography subsequent to venography can be of value in determining the nature of the lesion. Stenosis of the ureter usually indicates the presence of a malignant growth.

ZUSAMMENFASSUNG

Eine Beckenvenographie ist in 30 verifizierten Fällen durchgeführt worden. Normale Variationen, welche den in pathologischen Fällen beobachteten ähneln, werden auf der Grundlage von 9 verifizierten negativen Fällen besprochen. Pathologische Veränderungen in der Form von Verlagerungen und Einkerbungen, mit oder ohne haemodynamische Veränderungen, wurden in 17 von 21 verifizierten positiven Fällen beobachtet. Die Venographie ist ein wertvolles Supplement für andere Methoden, um expansive Erkrankungen im knöchernen Becken zu diagnostizieren und in einigen Fällen ist sie das einzige Mittel, deren Vorhandensein festzustellen. Eine Urographie im Anschluss an die Venographie kann für die Bestimmung der Art der Erkrankung von Wert sein. Ureterstenose zeigt gewöhnlich das Vorhandensein einer bösartigen Geschwulst an.

RÉSUMÉ

L'auteur a pratiqué une phlébographie pelvienne dans 30 cas vérifiés. Il examine les variations normales semblables à des images trouvées dans des cas pathologiques d'après une série de 9 cas normaux vérifiés. Il a observé des modifications pathologiques, déplacement, indentation, avec ou sans modification de l'hémodynamique, dans 17 sur 21 cas positifs vérifiés. La phlébographie est un appoint de valeur pour le diagnostic des tumeurs pelviennes et fournit dans certains cas le seul moyen d'affirmer leur présence. L'urographie qui suit la phlébographie peut être utile pour déterminer la nature de la lésion. Une sténose de l'uretère indique habituellement la présence d'une tumeur maligne.

REFERENCES

1. Abeshouse, B. S. and Ruben, M. E.: Prostatic and periprostatic phlebography. J. Urol. 68 (1952), 640.
2. Baux, R. et Poulhes, J.: Technique de la phlébographie pelvienne. Presse méd. 58 (1950), 451.
3. Begg, A. C.: Intraosseous venography of the lower limb and pelvis. Brit. J. Radiol. 27 (1954), 318.
4. De La Pena, A.: Röntgendarstellung der Gefässe des Beckens beim Manne. Z. Urol. 43 (1950), 474.
5. Drasnar, V.: Intraspongiöse Dauertropfinfusion. Schweiz. med. Wschr. 76 (1946), 36.
6. Ducuing, J., Guilhem, P., Marquès, P., Baux, R. et Paille, J.: Résultats des phlébographies du bassin et des membres inférieurs dans les cancers pelviens urogénitaux. Bull. Ass. France Cancer 38 (1951), 512.
7. Fariñas, P. L.: Abdominal venography. Am. J. Roentgenol. 58 (1947), 599.
8. Fitzpatrick, R. J. and Orr, L. M.: Pelvioprostatic venography; preliminary report. J. Urol. 68 (1952), 647.
9. Gansau, H.: Retrograde Füllung der Beckenvenen durch perkutane Punktion der Vena cava inferior. Chirurgie 26 (1955), 375.
10. Gumrich, H. and Kübler, E.: Das phlebographische Bild der Beckenvenensperren und deren Ursachen. Fortschr. Röntgenstr. 82 (1955), 757.
11. Helander, C. G. and Lindbom, Å.: Sacrolumbar venography. Acta radiol. 44 (1955), 410.
12. — Roentgen examination of the inferior vena cava in retroperitoneal expanding processes. Acta radiol. 45 (1956), 289.
13. — Personal communication.
14. Hilscher, W. M.: Die Phlebographie der tiefen Beckenvenen einschliesslich der Vena cava inferior. (Ein Erfahrungsbericht) Fortschr. Röntgenstr. 82 (1955), 741.
15. Kahr, E.: Darstellung der Beckenvenen mittels transossärer Serienphlebographie. Fortschr. Röntgenstr. 78 (1953), 449.
16. Petkovic, S.: Darstellung der Beckenvenen durch verschiedene Wege. Fortschr. Röntgenstr. 79 (1953), 739.
17. Seldinger, S. I.: Catheter replacement of the needle in percutaneous arteriography. A new technique. Acta radiol. 39 (1953), 368.
18. Süsse, H. J.: Gefahren und Technik der Osteomyelographie und transossalen Venographie. Fortschr. Röntgenstr. 85 (1956), 181.
19. Wanke, R. und Gumrich, H.: Chronische Beckenvenensperre. Zbl. Chir. 75 (1950), 1302.
20. Wellauer, V. J.: Beckenvenographie. *In:* Schinz, Glauner, Uehlinger: Röntgendiagnostik. Ergebnisse 1952—1956, p. 252. Georg Thieme, Stuttgart 1957.

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CHOLEGRAPHY WITH DEPRESSION OF THE RENAL EXCRETION OF THE CONTRAST MEDIUM

by

N. P. G. Edling and *C. G. Helander*

In cholegraphy the contrast medium (Biligrafin) is mainly eliminated through the liver and, to a lesser extent, through the kidneys. LANGECKER, HARWART & JUNKMANN (1952) state that 90 per cent of the medium is excreted by the liver and 10 per cent by the kidneys. According to LANGECKER (1956) the ratio of the excretion between the bile and urine is dependent upon the size of the dose; at a low concentration of the substance in the blood, that of the liver is greater, at a high concentration that of the kidneys. WITZGALL & TREBBIN (1955) have found that in liver disease 50 per cent of the medium may be eliminated through the kidneys. SHEHADI (1956) discusses the excretion at some length and states that in 90 per cent of his cases the contrast medium appeared in the bile ducts immediately after injection, while 10 per cent was excreted entirely by the kidneys. Simultaneous hepatic and renal excretion frequently occurred without evidence of liver disease and with satisfactory demonstration of the biliary tract. Also THEANDER (1956) has found that visualization of the renal pelvis does indicate hepato-biliary disease.

Combined hepatic and renal excretion is commonly observed when patients are prepared and dehydrated in the same manner as before urography

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a b

Fig. 1. Cholegraphies in one patient after cholecystectomy and sphincterotomy (40 ml Biligrafin 30 % on both occasions). a) 30 min after injection. Bile-ducts: filling of low density. Renal pelvis: high density. b) 35 min after injection of 10 ml PAH before the contrast medium. Bile-ducts: better filled. Renal pelvis: very low density.

and when high doses are given (Fig. 1a). The superimposed shadow of the right renal pelvis is at times of such density that assessment of the common duct becomes difficult. Moreover, its filling indicates that the renal excretion is interfering with the hepatic excretion. Although the excretion capacity of the liver cells is limited, preservation of the concentration of the contrast medium in the plasma will increase the excretion time.

The confusing superimposed shadows may be resolved by means of tomography.

For the purpose of reducing the renal excretion and increasing the hepatic excretion the writers have investigated the effect of paraminohippuric acid (PAH) in cholegraphy, utilizing their experiences in the reduction of the nephrographic effect in urography when the tubular excretion of the contrast medium is depressed by PAH, injected intravenously (EDLING, HELANDER & SELDINGER 1957). An injection of 10 ml PAH (20 % solution of sodium paraminohippuric acid) should precede the injection of Biligrafin. PAH is given through the same needle immediately before the latter, since the excretion time for the larger part of the PAH is 30 to 40 minutes, after which it loses its effect.

Table

Cholegraphies without and with depression of the renal excretion by means of PAH or Penditan. The figures in brackets denote the number of cases as a percentage.

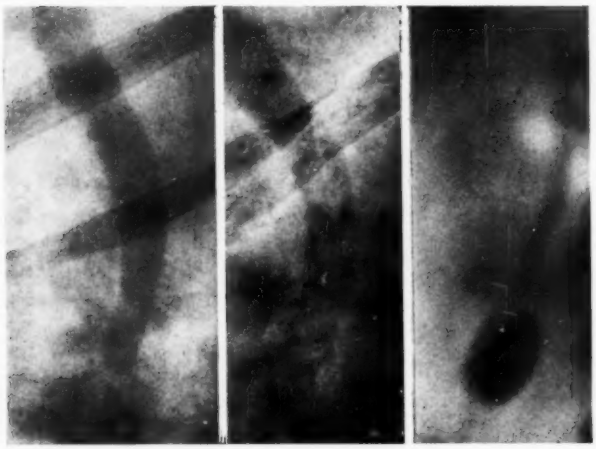
Depression	Number	Degree of density					
		Bile ducts			Renal pelvis		
		None	Low	High	None	Low	High
Without	92	1(1)	39(42)	52(57)	12(13)	52(56)	28(31)
PAH	82	4(5)	18(22)	60(73)	35(43)	32(39)	15(18)
Penditan....	51	3(6)	7(14)	41(80)	15(29)	26(51)	10(20)
PAH + Penditan..	3	—	—	3	2	1	—

Penicillin, like PAH, is also eliminated via the tubules of the kidneys and depresses the simultaneous excretion of an iodine compound. In order to protract its effect, penicillin may be combined with N,N'-dibenzylaethylendiamine to form an almost insoluble salt (Penditan — Kabi), which is only slowly absorbed after its injection intramuscularly. Penditan has also been used in a number of cases for depressing the renal excretion of Biligrafin. It is administered in a dose of 2 ml on the evening before the examination; the full effect is not obtained until after six hours, after which it lasts for more than 24 hours.

The dosage of Biligrafin was 20 or 40 ml, usually 40 ml, throughout the investigation. The 50 % solution was used more often than the 30% solution, the ordinary dose thus being 40 ml Biligrafin 'forte' (50%).

Films were obtained at intervals of 15 minutes over a period varying from one to one-and-a-half hours in cases which had undergone cholecystectomy, and for two hours in non-surgical cases. Special views in the supine, prone, or erect positions were obtained when indicated, in addition to the conventional films.

With due consideration for the safety of the patients a control series necessitating two examinations in the same case were ruled out. Instead, a number of cholegraphies, from a period before the depression of the tubular excretion had been initiated, were compared with a number from a period after it had started. The number of cholegraphies without depression of the renal excretion was 92. PAH was used for the depression in 82 cases, Penditan in 51, and both PAH and Penditan in 3 cases. The comparison of the materials includes the degree of filling of the bile-ducts and of the right renal pelvis. In the Table above the cholegraphies are brought together on this basis and divided into cases with no filling (none), with a low degree of density (low), and with a high degree of density (high). The different



a b c

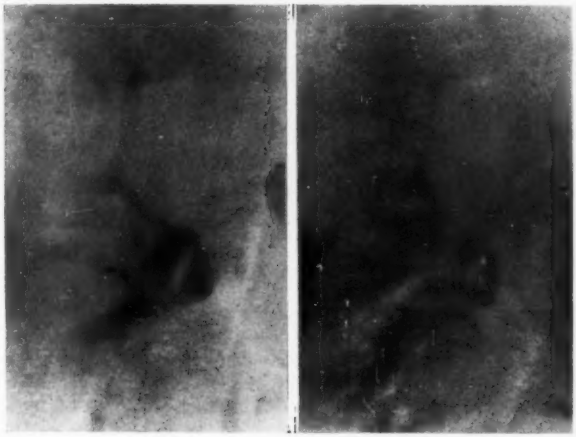
Fig. 2. a) and b) Two cholegraphies after cholecystectomy (10 ml PAH + 40 ml Biligrafin 30%). a) 25 min after injection. Bile-ducts: filling of fairly high density, slight dilatation. Renal pelvis: no filling. b) 45 min after injection. Bile-ducts: filling of low density, slight dilatation, defects in lower part of the common duct (at re-operation, 7 gallstones were found). Renal pelvis: no filling. c) Cholegraphy and tomography (10 ml of PAH + 40 ml of Biligrafin 50%). Bile-ducts: filling of high density, diverticula in medial wall of common duct, filled before the contrast medium had entered duodenum. Renal pelvis: no filling. Cholangiography during operation again showed the diverticula.

degrees of density in the bile-ducts and in the renal pelvis are of course not comparable; they refer to low and high degrees of density in cholegraphy and in urography, respectively. The figures in brackets are the numbers as percentages. Since most patients with severe liver damage are not sent for cholegraphy, there are only a few cases recorded with no ecxretion of contrast medium into the bile-ducts.

The figures in the Table indicate that with a depression of renal excretion in cholegraphy the percentage of cases with a higher degree of density in the bile-ducts is greater than it is without depression, and that the percentage of cases with a lower degree of density in the renal pelvis is also greater. Both these facts facilitate the assessment of the biliary ducts (Figs. 1 and 2).

The three cholegraphies with Penditan and PAH combined as depressants do not necessarily permit of any conclusions. They merely show that the findings agree with the series in which depressions was obtained either with Penditan or PAH.

In the series with depressants, Penditan produced a higher density in the bile-ducts in a greater percentage of cases than did PAH; the latter,



a b

Fig. 3. Cholegraphy in liver disease (alkaline phosphatases 14). (2 ml Penditan + 10 ml PAH + 40 ml Biligrafin 50%). a) 5 min b) 2 hours after injection. No hepatic excretion. Renal excretion throughout decreasing. Alkaline phosphatases unchanged 3, 12, and 32 days, respectively, after examination.

on the other hand, checked the excretion of the contrast medium by the kidneys in a greater percentage of cases. It is probable that the latter observation may be explained by the fact that PAH has its maximum effect during the same time as most of the contrast medium is excreted.

It will also be seen from the Table that in cholegraphy without depression the contrast medium was eliminated by the renal route in as many as 87 per cent of the cases: the bile-ducts were filled with low or high density in 99 per cent.

In the group of patients given injections of PAH in the above-stated dose, no complications which could be related to the injection were encountered. In no case with depression of the renal excretion did signs of a disturbed liver function appear, nor any change for the worse when the liver function was already impaired (Fig. 3). It may also be noted that the depression of the tubular excretion of the contrast medium is not absolute, and that the glomerular filtration is intact.

Since the compared materials are not selected, with the exception of the depressing compounds, no consideration is given to clinical findings of hepatic or renal signs.

The most effective depression is of course obtained by the injection of Penditan and PAH combined. (See the Table.) As has been stated, Penditan must be injected intramuscularly at least six hours before the examination. It is administered to in-patients on the previous evening in the

ward; for out-patients the injection necessitates an extra visit to the hospital. For this reason, it is in general most expedient to inject PAH intravenously, which is done in the roentgen department, and in special cases to use both Penditan and PAH.

Probenecid (p-/dipropylsylfamyl/-benzoic acid) may be given instead of Penditan. The substance greatly reduces the tubular excretion and has therefore been added to benzyl penicillin to protract its effect. It is administered by the oral route. Probenecid has not been tried in the present material.

SUMMARY

Cholegraphies with and without depression of the renal excretion of the contrast medium after administration of PAH or Penditan have been compared in a total material of 228 cases. It was found that in the series with a depressant the percentage of cases with high density in the bile-ducts and low density in the right renal pelvis was greater than in the controls. Assessment of the bile-ducts is facilitated by the employment of these substances in cholegraphies.

ZUSAMMENFASSUNG

Cholegraphien mit und ohne Herabsetzung der Nierenausscheidung des Kontrastmittels nach Verabreichung von PAH oder Penditan sind in einem Gesamtmaterial von 228 Fällen miteinander verglichen worden. Man fand dass in Serien mit einer Herabsetzung der Prozentsatz von Fällen mit grosser Kontrastdichte in den Gallengängen und geringer Dichte im rechten Nierenbecken grosser war als im Vergleichsmaterial. Die Beurteilung der Gallenwege wird durch Benutzung dieser Substanzen bei Cholegraphien erleichtert.

RÉSUMÉ

Sur une série totale de 228 cas, les auteurs ont comparé des cholégraphies avec et sans dépression de l'excrétion rénale du moyen de contraste après administration de PAH ou de Penditan. Ils ont constaté que, dans la série ayant reçu un dépresseur, le pourcentage de cas présentant une forte opacité des voies biliaires et une faible opacité dans le bassinet du rein droit était plus élevé que chez les sujets de contrôle. L'examen des voies biliaires est facilité par l'emploi de ces substances dans les cholégraphies.

REFERENCES

EDLING, N. P. G., HELANDER, C. G. and SELDINGER, S. I.: The nephrographic effect in depressed tubular excretion of Umbradil. Acta radiol. 48 (1957), 1.

HARWART, A. und JUNKMANN, K.: quoted by PRÉVÔT.

HORNYKIEWYTSCH, TH.: Intravenöse Cholangiographie. Georg Thieme Verlag, Stuttgart 1956.

LANGECKER, H.: *In:* HORNYKIEWYTSCH: Intravenöse Cholangiographie.

PRÉVÔT, R.: Die Cholangiographie mit Biligrafin. *In:* H. R. SCHINZ, R. GLAUNER und E. UEHLINGER: Röntgendiagnostik. Ergebnisse 1952—1956, p. 491. Georg Thieme Verlag, Stuttgart 1956.

SHEHADI, W. R.: Recent advances in the roentgen visualization of the biliary tract. Indian J. Radiol. 1956. Souvenir number.

THEANDER, G.: On the visualization of the renal pelves in cholegraphy. Acta radiol. 45 (1956), 283.

WITZGALL, H. und TREBBIN, U.: quoted by PRÉVÔT.

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ROENTGENOGRAPHIC STUDIES OF CUTANEOUS AND SUBCUTANEOUS INFILTRATES IN ERYTHEMA INDURATUM AND ERYTHEMA NODOSUM

by

C. G. Leczinsky and *O. Mattsson*

Studies of subcutaneous infiltrates, on which one of us (LECZINSKY) has been engaged, mainly from the dermatologic standpoint, gave rise to the idea of trying soft-tissue roentgenography as an aid to diagnosis. The literature contains only sparse reports on roentgenographic examinations of cutaneous and subcutaneous formations. BONSE (1952) made observations on the roentgenographic appearances of erythema induratum. He distinguished two types: well-defined nodules as manifestations of a productive process, and small ill-defined infiltrates which would correspond to an exudative process. He also compared the appearances with those seen in pulmonary tuberculosis and found a striking correspondence. Such a comparison seems difficult to understand.

Methods previously used for producing roentgenograms of soft tissues have not been satisfactory, the contrast leaving much to be desired. FRANTZELL (1951) threw light upon some of the problems of soft-tissue roentgenography, and the technique has now been further improved.

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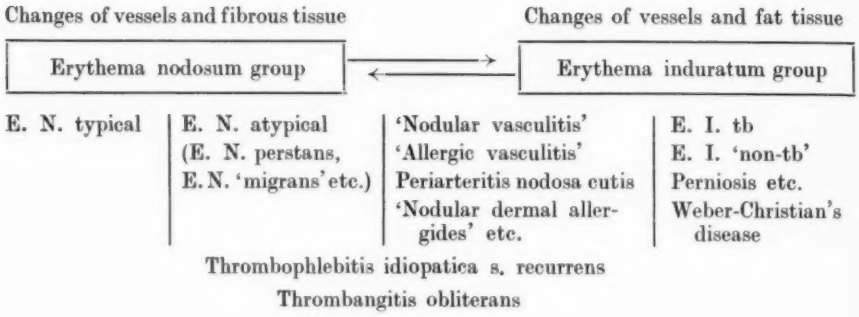
Since the image intensifier has come into use in roentgen departments, essential improvement in the quality of the image has been possible, as has been shown by one of us (MATTSSON 1956), by the selective screening of the primary radiation. The method of using the image intensifier as an aid to centering in soft-tissue techniques has given particularly good results.

Our material consists of subcutaneous infiltrates on the legs. From the viewpoint of the survey, the types of pertinent histological changes can be divided into two main groups, which will be designated as the erythema nodosum and erythema induratum types. There are, of course, variants of these two groups, and also intermediary forms, as illustrated below:



In this investigation we have studied the structure of the subcutis and have disregarded the vascular changes which are nearly always present, as well as the cytology, and the finer histologic structures. These aspects, as well as the aetiology, pathogenesis, and clinical manifestations, will be dealt with in another work. Nor will the many attempts at systematizing various forms of panniculitis, which have been made in the course of years be discussed in the present paper.

The histologic picture in the erythema nodosum types, nodular vasculitis (MONTGOMERY et coll. 1945, and others), some cutaneous forms of periarteritis nodosa, erythema nodosum 'migrans' (BÄFVERSTEDT 1954), and erythema nodosum perstans, may be described as follows (after LÖFGREN and WALLGREN 1949).

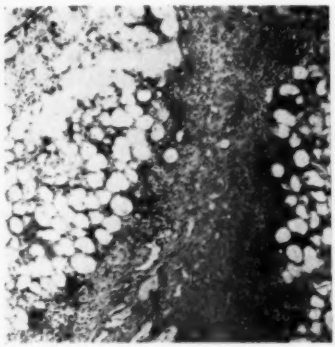


Fig. 1. Thickened septum in a case of erythema nodosum of long duration. × 250.

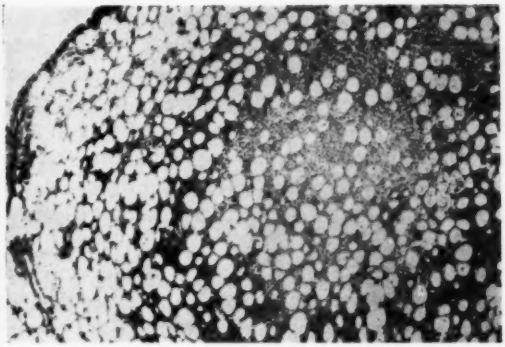


Fig. 2. Erythema induratum. Slender septa and involvement of fatty tissue. × 250.

The changes mainly involve the deeper layers of the dermis and the fibrous septa between the fat lobules (see Fig. 1). The tissues are here the seat of oedema, cellular infiltration, and haemorrhages, and the collagen undergoes fibrinoid degeneration. The histologic appearance of the changes differs according to the age of the efflorescence. Fig. 1 shows a detail of a specimen demonstrating a thickened septum in a case of erythema nodosum of long duration. The above-mentioned tissue elements, however, are involved to a much higher degree than is the fatty tissue itself in which frequently 'Wucher' atrophy is seen in areas nearest the septa. Necrosis of the fatty tissue accompanied by atrophy does not occur, and the final stage is complete restoration to a healthy condition.

The erythema induratum type here refers not only to forms of panniculitis associated with tuberculosis and of a tuberculous structure, but also to erythema induratum 'non-tb' (WHITFIELD 1901), Darier's subcutaneous sarcoid, Weber-Christian's disease in certain stages, and several similar affections.

In erythema induratum the structure is in the main different from that described above for erythema nodosum. The vascular changes predominate, and the picture of panniculitis may be conditioned by these changes but is, undoubtedly, in many cases primary. The changes begin in the fat lobules in which granulomatosis of lipoid tissue is seen (often of a tuberculoid type), and in many instances there are areas with coagulation and caseous necrosis. The fibrous septa, on the other hand, are less involved and may remain slender. (See Fig. 2.) As a whole, the tissue histologically appears more solid than in erythema nodosum, and mostly large portions of unchanged or slightly changed fatty tissue are seen.

The roentgen technique was as follows. The skin eruptions were recorded with a tangential beam. To achieve this, an indicator was applied to the centre of the affected skin surface. The central beam could easily be adjusted in relation to the efflorescence under fluoroscopic control with the image intensifier, and, by means of a special variable diaphragm, the irradiated field could be selectively reduced to a minimum. In this way the amount of secondary radiation as well as the so-called extra-focal radiation were also reduced with resultant improvement in the quality of the image.

A kilovoltage of from 40 to 50 was selected and the recording made on a non-screen film, which afforded the best definition; Gevaert Osray film was normally used. A routine roentgen processing technique was employed.

The 20 cases in our series, which form part of a larger material, were examined during 1955 largely in the order in which they attended the Dermatologic Clinic; there was thus no selection. All were fully investigated clinically, and with special regard to tuberculosis, other infections, and circulatory disorders. Histologic examination was carried out in all cases excepting two. These two, however, exhibited typical clinical pictures and should be included in the investigation. Of the 20 patients, 18 were women and 2 men. Seven cases were erythema nodosum type, 9 of the erythema induratum type, and 4 of intermediary forms. All the seven cases in the first mentioned group, 6 of the group erythema induratum, and all the 4 cases in the intermediary group are described in the case reports.

The classification of the diseases discussed in this paper is given according to the inter-relationships between the different types of subcutaneous infiltrates, indicated on p. 194. The extreme histologic and clinical erythema nodosum and erythema induratum types pass without any distinct line of separation into other conditions which have been given various designations, and in which — besides panniculitis — the vascular changes usually predominate.

The roentgenographic appearances in the first of the two main groups, erythema nodosum, may be characterized as follows (Cf. Fig. 3).

The cutis is distinctly thickened in the area of efflorescence. Its lower border against the subcutis is indistinct, and the cutis passes gradually into a net-work of fairly coarse fibres. Small meshes are bound by coarse threadlike septa; peripherally and towards the deep layers the lesion merges successively into normal tissue with very sparse and slender septa. The lower margin of the cutis and its transition into septa presents a picture reminiscent of a fringed edge of a piece of cloth or the surface of a coarse blanket.

The clearly visible septa probably correspond to the histologically changed connective tissue areas, including the vessels. All septa histologically verifiable may, of course, not be seen in the roentgenogram which is a summation effect. The small areas of fatty tissue observable between them are fairly regular in size and shape. As has been mentioned above, the fatty tissue in these areas is as a rule also slightly involved.

The roentgenographic examination of the second main group, erythema induratum, shows the following characteristic features. (Cf. Figs. 4 and 5.) In contradistinction to the previous group the thickened cutis at the site of efflorescence shows a distinct, well discernible line of separation from the subcutis. As was mentioned for the erythema nodosum group, the lower contour of the cutis presents a fringe-like appearance, which possibly corresponds to the point of origin of the thickened septa. In accordance with what has been said in connection with the histologic picture, the septa in the erythema induratum group are slender and less marked and therefore cannot be expected to appear equally distinctly. The subcutis appears with diffusely increased density, as in oedema with infiltration. Connective tissue of regular appearance can no longer be seen; marked, dense bands without regularity are occasionally observed, and these possibly correspond to the course of the subcutaneous vessels.

When the contour of the skin shows an indentation, this suggests the presence of atrophy corresponding to late stages of pathologic changes in the fatty tissue, as in Case 17, for instance.

Cases 14 to 17 cannot reasonably be referred to either the erythema nodosum or the erythema induratum groups and have therefore been designated as intermediary forms. Their place in the system lies between the two extreme groups. Cases 14 and 15 come near to the erythema nodosum group, while Cases 16 and 17 show greater similarity with the erythema induratum group.

Clinical data and histologic findings are included in the following brief case reports (p. 198 to 203).

From our observations it seems possible that the roentgenographic examination may provide a means of separating, with a fair degree of probability, the two main types of panniculitis. We have noticed the obvious conformity between what is revealed in the roentgenograms and what is known about the anatomic structures.

Case reports

Cases of the erythema nodosum group (Fig. 3).

Case 1. Woman, aged 44, who since 1953 had experienced periods of fever and efflorescenses on the arms and legs of the erythema multiformae and erythema nodosum types. The last attack occurred in 1955 when she had solitary eruptions, clinically and histologically of the last mentioned type; these were investigated by soft-tissue roentgen ography.

Case 2. Man, aged 50, who since 1949 had recurrent infiltrates on the legs, situated cutaneously and superficially subcutaneously. Clinically nearest to the erythema nodosum type. Most of them resolved without scars or areas of atrophy. *Histology:* In addition to severe vascular changes, a structure most like that of erythema nodosum in the early stages, while lesions in late stages showed no specific features.

Case 3. Woman, aged 42. Attacks of erythema nodosum appeared in the second month of three pregnancies, the last one in 1954. Firm, red infiltrates of this type on the anterior and postericr surfaces of the legs. *Histology:* Vascular changes. Fibrinous septa with fibrinoid degeneration; very slight cellular infiltration in subcutaneous fat tissue.

Case 4. Woman, aged 37. One or two attacks of solitary eruptions on the legs, clinically and histologically of the erythema nodosum type. No evidence of tuberculosis or focal infections. The eruptions resolved after rest without leaving any visible traces.

Case 5. Woman, aged 35, who had infiltrates on the legs of the erythema nodosum type, with recurrences for 9 months in 1955. No evidence of tuberculosis or focal infections. Clinically typical erythema nodosum. Healing occurred without any visible traces.

Case 6. Man, aged 35, admitted with erythema nodosum lesions on the legs. Chest film showed enlarged hilar structures. Mantoux reaction negative. His condition was interpreted as Schaumann's disease.

Case 7. Woman, aged 33, who since middle of 1955 had recurrent nodules on left leg. No history or evidence of tuberculosis. *Histology:* Erythema nodosum.

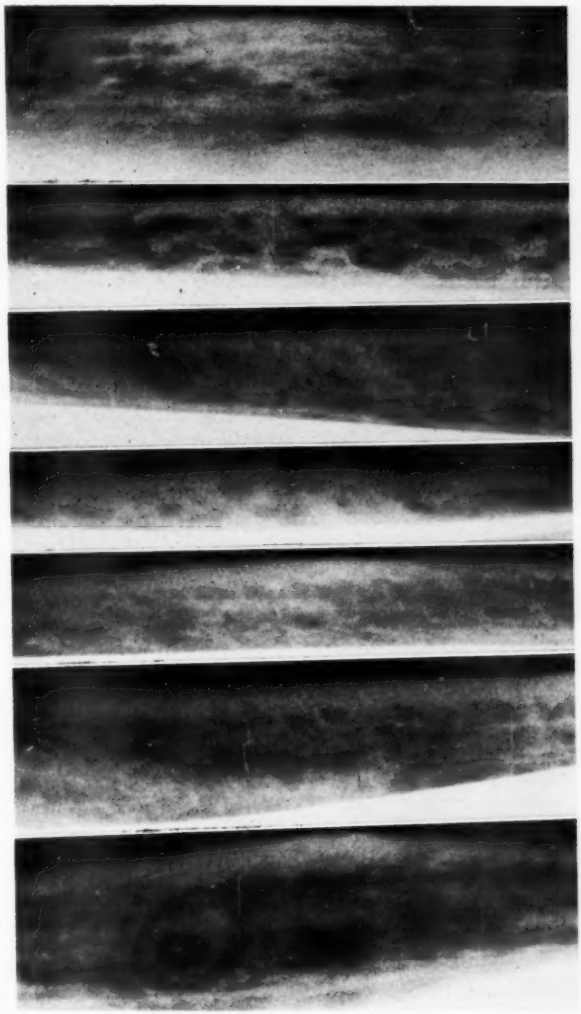


Fig. 3. Cases 1 to 7. Erythema nodosum type. Thickened cutis with irregular border against subcutis. Prominent 'septa' limiting fat lobules.

Cases of the erythema induratum group (Fig. 4).

Case 8. Woman, aged 40. Tuberculous spondylitis in 1942. Since about 1945 recurrent well-defined and tender infiltrates, the size of peas, on the legs, mainly involving the subcutis. *Histology:* Only lesions in an early stage were examined, these showing vascular changes but no marked panniculitis. The case was placed in this group because of the history and the clinical manifestations.

Case 9. Woman, aged 67, who had recurrent infiltrates on the legs since 1950. The clinical picture was also that of erythema induratum and was confirmed by biopsy. Scars and areas of atrophy were present in addition to tender, reddened cutaneous-subcutaneous infiltrates.

Case 10. Woman, aged 35, who since 1948 had attacks of cyanotic, at times ulcerating, infiltrates on the legs; these had healed leaving scars and areas of atrophy. No evidence of tuberculosis apart from a calcified primary lesion in the lungs and a positive Mantoux reaction. *Histology:* Marked vascular changes. Some patches of panniculitis in the process of breaking down, most marked between the cutis and the subcutis. Clinically and histologically of the erythema induratum type.

Case 11. Woman, aged 48, had from her 33rd year never been free from recurrent tender infiltrates, at times ulcerating, on the legs. Family history of tuberculosis and scrophulosis. Recurrent pharyngitis. *Histology:* Changes principally of the erythema induratum type.

Case 12. Woman, aged 45, with infiltrates on the legs, which had appeared in connection with angina simplex in 1941, and then of the erythema nodosum type. Later she had patches of panniculitis on the legs as well as in the gluteal region, often accompanied by joint pains and occasional ulceration. *Histology:* The changes mainly involved the fatty tissue, being thus principally of the erythema induratum type.

Case 13. Woman, aged 43, who since 1930 had repeated attacks of infiltrates on the lower part of the legs, diagnosed and treated as erythema induratum. *Histology:* Erythema induratum.

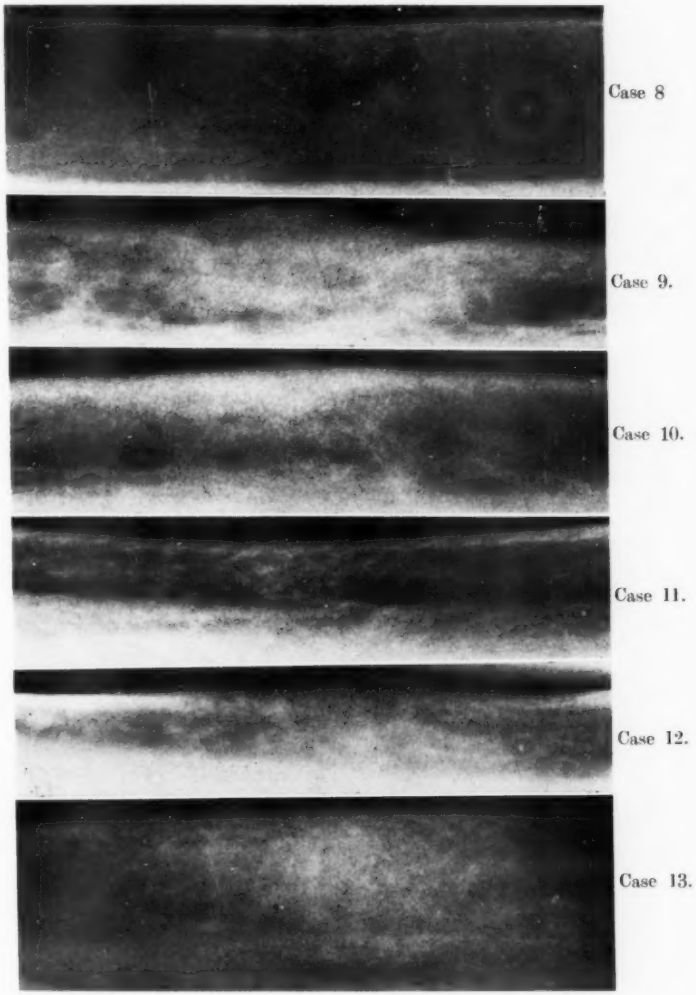


Fig. 4. Cases 8 to 13. Erythema induratum type. Moderately thickened cutis with definite border line against the subcutis, which appears diffusely increased in density.

Cases of the intermediary group (Fig. 5).

Case 14. Woman, aged 42, who since 1953 had several attacks of infiltrates on the calfs. No evidence of tuberculosis; signs of dental sepsis; chronic chillblains. Infiltrates as large as the palm of a child's hand present on the calfs. *Histology:* Marked 'Wucher' atrophy in the subcutis; areas with considerable thickening of the vascular walls. Rounded lesions in a few places; no tuberculoid structure; haemorrhages; fairly marked congestion. No specific histologic picture but one interpreted as erythema nodosum in a later stage than erythema induratum. Probably of an intermediary type.

Case 15. Woman, aged 47. Erythema nodosum at the age of 7. History of intermittent infections and hormonal deficiency (salpingo-oophorectomy). Panniculitis appeared in 1940, attacking the mammae and later the buttocks. During the past few years unchanged cutaneous — subcutaneous infiltrates of partly annular distribution over the calfs, not responsive to treatment. No areas of atrophy. The clinical appearance was that of erythema nodosum chronicum migrans (BÄFVERSTEDT). *Histology:* Erythema nodosum type of long duration with marked granulomatosis of fatty tissue.

Case 16. Woman, aged 27, who during two pregnancies had infiltrates on the legs, clinically of the erythema nodosum type, partly with a migratory course. *Histology:* Predominantly of the erythema nodosum type, but also with some lesions in the process of melting, that is, phenomena included in the erythema induratum picture. The case seemed to be of an intermediary type.

Case 17. Woman, aged 34. One or two attacks of infiltrates on the legs, clinically and histologically of the erythema nodosum type. During later attacks of infiltrates, ulceration also occurred (Arthus' phenomenon); the lesions retained their clinical erythema nodosum type, but histologically, all the tissue elements were increasingly involved and the case was judged as being of an intermediary form.

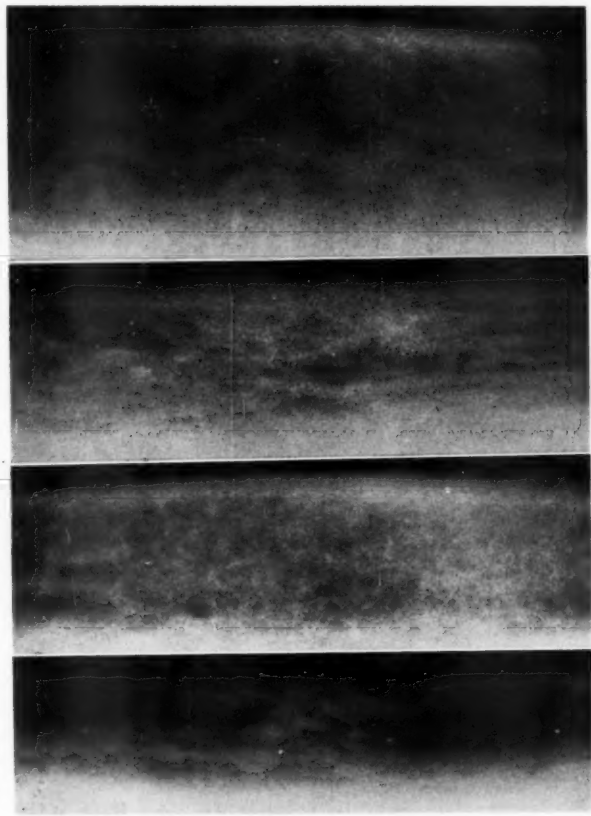


Fig. 5. Cases 14 to 17. Intermediary group, of which 14 and 15 are similar to the erythema nodosum group, and 16 and 17 simular to the erythema induratum group.

SUMMARY

Twenty cases of panniculitis of the lower legs have been examined roentgenographically and the results studied with special regard to the differential diagnosis. Typical roentgenographic appearances were found in two main types of subcutaneous changes, which have been called the erythema nodosum and erythema induratum groups.

ZUSAMMENFASSUNG

Zwanzig Fälle mit Panniculitis der unteren Extremitäten sind röntgenologisch untersucht worden. Die Resultaten wurden unter besonderer Berücksichtigung der Differentialdiagnose studiert. Typische röntgenologische Befunde lagen bei 2 Haupttypen von subkutanen Veränderungen vor; diese sind als Erythema Nodosumgruppe und als Erythema Induratumgruppe bezeichnet worden.

RÉSUMÉ

Vingt cas de panniculite des membres inférieurs ont été examinés radiographiquement et les résultats ont été étudiés spécialement au point de vue du diagnostic différentiel. On a trouvé des aspects radiographiques typiques dans deux principaux types de lésions souscutanées qui ont été appelés groupe de l'érythème noueux et groupe de l'érythème induré.

REFERENCES

Bonse, G.: Zur Kenntnis des Erythema induratum Bazin im Weichstrahlröntgenbild. Arch. Derm. Syph. 193 (1952), 579.

— Anwendungsmöglichkeiten röntgenologischer Weichteildiagnostik ohne Kontrastmittel. Fortschr. Röntgenstr. 74 (1951), 450.

— Zur Röntgenweichstrahldiagnostik der tertiären Lues der Haut. Arch. Derm. Syph. 195 (1952), 96.

— und Karg, R.: Röntgenbefunde bei Angiomatosis Kaposi. Fortschr. Röntgenstr. 78 (1953), 456.

Bäfverstedt, B.: Erythema nodosum migrans. Acta. derm.-venereol. 34 (1954), 181.

Frantzell, A.: Soft tissue radiography. Acta radiol. Suppl. 85 (1951).

Leczinsky, C. G.: Preliminary report in Proc. XI. Internat. Congr. Derm, 1957. (In press.)

Löfgren, S. and Wallgren, F.: On the histopathology of erythema nodosum. Acta derm.-venereol. 29 (1949), 1.

Mattsson, O.: Preliminary report in Proc. Swed. Ass. Med. Radiol. (In Swedish.) Nord.Med. 55 (1956), 343.

Montgomery, H., O'Leary, P. A. and Barker, N. W.: Nodular vascular diseases of the leg. J. A. M. A. 128 (1945), 335.

Whitfield, A.: On the nature of the disease known as erythema induratum scrophulosorum. Am. J. Med. Science 122 (1901), 828.

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ROENTGENOLOGIC FINDINGS IN FIVE CASES OF CONGENITAL ANEURYSM OF THE AORTIC SINUSES (SINUSES OF VALSALVA)

by

H. Gösta Davidsen, Olaf Petersen, and *Gregers Thomsen*

Congenital aneurysm of the aortic sinuses of Valsalva represent a cardiac lesion which is seldom diagnosed in vivo, possibly because the symptoms are quite mild in the uncomplicated case. Complications in the form of rupture into the chambers of the heart, compression of the bundle of His, secondary bacterial endocarditis, or impairment of aortic valvular function, are potential dangers in all cases of aortic sinus aneurysm.

As the prognosis following the occurrence of a rupture into the heart is extremely bad, attempts have been made to close the communication between the aorta and the right heart (Oram & East 1955, Husfeldt & Davidsen 1956). However, such attempts have so far proved unsuccessful, and both the patients operated upon died on the table. Although the operative risk must be high in such cases, the poor prognosis will justify future attempts at achieving surgical repair. The success of future surgical intervention will probably depend partly on the use of extracorporeal circulation with an artificial heart and oxygenator, and partly on a care-

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ful selection of the cases. The operability of different types of aneurysm has been discussed by DAVIDSEN, FABRICIUS & HUSFELDT 1958 on the basis of a study of the literature. The indications for surgery were regarded as being limited to cases in which a rupture of an aneurysm into the right heart had been followed by a considerable left-to-right shunt. Cases presenting one of the following complications: endocarditis, syphilis, arteriosclerosis, or an intraventricular septal defect, were regarded as less amenable to surgery.

The clinical picture of a ruptured sinus aneurysm is so characteristic that the diagnosis can be suspected from the clinical examination in nearly every case; on the other hand, this picture is not pathognomonic of ruptured sinus aneurysms and the underlying lesion may show numerous variations, the differentiation of which will demand an intensive combination of cardiologic and roentgenologic diagnostic methods.

In typical cases the rupture occurs as a dramatic episode in a subject who has never previously had any cardiac symptoms. Rupture may occur at any age, but is rarely seen before adult life has been reached. A sudden choking sensation in the chest combined with pain behind the sternum is the common initial symptom. Dyspnoea or orthopnoea is present in the early stages, and commonly the patient runs a moderate increase of temperature during the first few days. An increasing degree of decompensation of the heart follows, until a final stage of anasarca with ascites and pleural effusion is reached. In about 50 % of cases death occurs before the end of the second month and very few will survive for more than 3 years (DAVIDSEN, FABRICIUS & HUSFELDT 1958).

On clinical examination the most typical finding is that of a loud systolic/diastolic or continuous machinery murmur heard in the region of the lower half of sternum close to the thoracic wall. A high pulse amplitude and a pistol-shot sound over the femoral artery are commonly present. Cases with these signs and symptoms should always be referred to a cardiac centre for angiocardiography and aortography in order to determine the size and localization of the aneurysm.

Present material

Owing to the rarity of the disease only a limited experience of this syndrome can be gained even in the larger cardiac centres. We therefore considered that publication of the roentgenologic findings in five cases observed in our hospital would be of interest. The 5 cases may be subdivided into three types according to the haemodynamic findings.

1. In Cases 1 and 2 there was a communication between the aortic sinus and the right heart. The left-to-right shunt passing through the com-

munication was added to the returning systemic venous blood and caused an equal increase of the flow through the right heart, the pulmonary circulation, and the left heart. The factor by which the ventricular flow work had been increased, was therefore identical with the figure 'pulmonary flow rate' (*i. e.* total pulmonary flow : effective circulation) which, when calculated according to the formulae of DAVIDSEN 1957, amounted to 2.0 and 3.3 in Cases 1 and 2 respectively. This means that the flow through both sides of the heart was increased 2.0 and 3.3 times in the two cases respectively.

2. In Cases 3 and 4 there was a back-flow of blood from the aorta to the left ventricle with haemodynamic consequences which were similar to those found in aortic valvular incompetence. The extra flow in these cases was confined to the left ventricle exclusively. The increase of the flow could not be measured, but regurgitation to the left ventricle was revealed at aortography.

3. No demonstrable haemodynamic abnormalities were present in Case 5.

A detailed clinical description of the cases is found in the paper of DAVIDSEN, FABRICIUS and HUSFELDT 1958, and below will be found a summary of the relevant data together with a description of the roentgenologic findings.

Case reports

Case 1. C. L. 317. Male bus driver born in 1917. [illegible]c murmur discovered in 1934 Heart catheterization in 1949 demonstrated a shunt to the right atrium, and an atrial septal defect was suspected despite the atypical findings of loud systolic and diastolic murmurs in the 2nd right and 4th left intercostal spaces. At a follow-up examination in 1956 further cardiac catheterization showed that the shunt was unchanged and that the pressures in the right side of the heart were still completely normal.

Roentgen examination of the chest (Fig. 1) revealed a bilateral enlargement of the heart with moderate prominence of the pulmonary artery. The pulmonary vascular markings were slightly increased. From the time of the first examination 7 years previously the cardio-thoracic ratio had increased from 17.7 : 30 cm to 20.5 : 31 cm, but there was no significant change in the shape of the heart.

Thoracic aortography was performed. The contrast medium was injected through a polyethylene catheter introduced percutaneously by a technique (THOMSEN & HANSEN 1954) which was a slight modification of the method described by SELDINGER 1953. The tip of the catheter had not been placed deeply enough in the root of the aorta, and, therefore, all the sinuses were not outlined by the contrast medium. Only in a right-sided sinus was the contrast medium retained for a short period, and it could be seen that the sinus was considerably dilated. On account of the poor filling, and with the rather small shunt present no demonstration of the right heart was possible. The diagnosis in this case was thus based on a typical murmur, a shunt into the right atrium and the right ventricle, and a demonstration of an enlargement of a right aortic sinus.

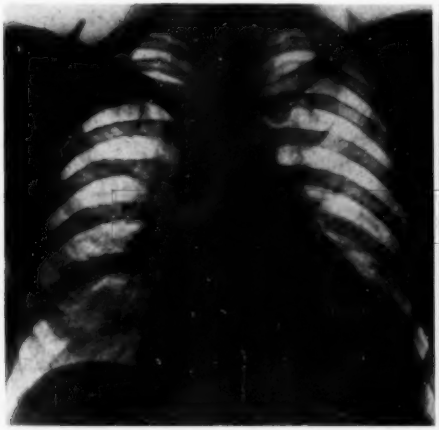

Fig. 1

Fig. 2

Figs. 1 and 2. Cases 1 and 2. P.a.-projection. Bilateral cardiac enlargement corresponding to an increased cardiac output from both ventricles.

Case 2. C. L. 3475. Female, born in 1930. At the age of 25 a sudden episode occurred during sleep and she awoke with palpitations, orthopnoea, and a feeling of anxiety. The symptoms increased, and she was referred to us 4 weeks later owing to the discovery of a loud machinery murmur, which could be heard over the lower end of the sternum. A rupture of one of the sinuses of Valsalva was suspected, and further support was given to this view when the presence of a shunt into the right atrium was demonstrated by cardiac catheterization.

Roentgen examination of the chest (Fig. 2) revealed bilateral enlargement of the heart and a heart silhouette very similar to that demonstrated in Case 1. The cardio-thoracic ratio increased from 14.5 : 26.5 cm to 17 : 27 cm during the period between 6 and 66 days after the acute onset of symptoms.

Angiocardiography was performed and showed that there was no significant hypertrophy, but that considerable dilatation of the right atrium and the right ventricle was present. At *thoracic aortography*, marked dilatation of the right anterior aortic sinus was demonstrated (Fig. 3). A small pouch at the lower margin of the sinus was filled with contrast medium, and slight contrast-filling of the right atrium was observed.

Surgical closure of the communication was attempted, but the patient died during the operation (Husfeldt & Davidsen 1956). Autopsy confirmed the presence of an aneurysm projecting as a pouch into the right atrium and having a rupture through which blood had flooded from the aorta into the right atrium. There was a bicuspid aortic valve containing a large anterior and a smaller posterior cusp and corresponding sinuses. The aneurysm had originated from the anterior sinus and had not interfered with the orifice of the right coronary artery.

Case 3. C. L. 422. A boy, born in 1944, was referred for examination following the finding of loud systolic and diastolic murmurs at the upper end of the left sternal border. Cardiac catheterization had been performed at the ages of 6 and 8 years and had demonstrated that no shunts were present and that the pressures in the right side of the heart and in the pulmonary artery were completely normal.

Roentgen examination of the chest (Fig. 4) showed that the heart was moderately enlarged to the left. The shape was rounded, and there was no prominence of the pulmonary artery nor any increase in the pulmonary vascular markings. The transverse cardiothoracic ratio was 11.5 : 22 cm.

By *angiocardiography*, performed at the age of 6 years, it had been demonstrated that the passage of the contrast medium through the chambers of the heart was normal. There was, however, an abnormal finding in that the origin of the pulmonary artery was posterior to the root of the aorta. Accordingly the latter was situated closer to the sternum than is generally the case. The left ventricle was considerably enlarged.

At *thoracic aortography* (Figs. 6 and 7) performed at the age of 11 years, all three aortic sinuses became outlined. The right coronary sinus was dilated and communicated with a saccular cavity about 1 cm in size. There was a considerable regurgitation of contrast medium into the left ventricle, which may have been due to either perforation of the aneurysm or incompetence of the cusp related to the dilated sinus.

Fig. 3. Thoracic aortography in Case 2. Left lateral. Enlargement of anterior aortic sinus, pouch projecting downwards and anteriorly. Contrast medium in front of and slightly below the level of root of aorta. (Anatomic diagnosis: Bicuspid aortic valve with aneurysmal pouch projecting and opening into right atrium.)

Case 4. C. L. 3762. Boy, born in 1953. At the age of 29 months following an attack of whooping cough he was referred to us on account of the roentgenologic demonstration of cardiac enlargement. He had loud systolic and diastolic murmurs at the lower left sternal border, but no signs of cardiac failure. No shunts could be demonstrated by right heart catheterization, and the pressures in the right heart were normal. Left ventricular pressure was measured with a catheter introduced through the aorta. A small systolic pressure gradient was found to be present over the aortic valve, viz. 123 mm in the left ventricle and 110 mm in the aorta.

Roentgen examination of the chest (Fig. 5) revealed enlargement of the heart to the left and a cardio-thoracic ratio of 10 : 17 cm. The ascending aorta was broadened, but there was no evidence suggestive of an aortic aneurysm. There was no prominence of the pulmonary artery nor any increase in the pulmonary vascular markings.

At *angiocardiography* the left ventricle was found to be markedly hypertrophied and dilated. There were no visible shunts. The chambers of the right side of the heart, the pulmonary artery, and the left atrium were opacified in regular order, and all were of normal size. *Thoracic aortography* (Figs. 8 and 9) was performed by the percutaneous introduction of a polyethylene catheter via the femoral artery. Three aortic sinuses were clearly outlined. Two of them, the left coronary and the posterior or non-coronary sinuses, were dilated and projected into the heart shadow, the former towards the left side and the latter towards the apex. The coronary arteries were seen to be normal in size and origin.

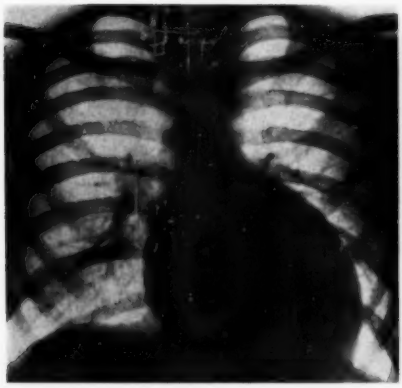

Fig. 4

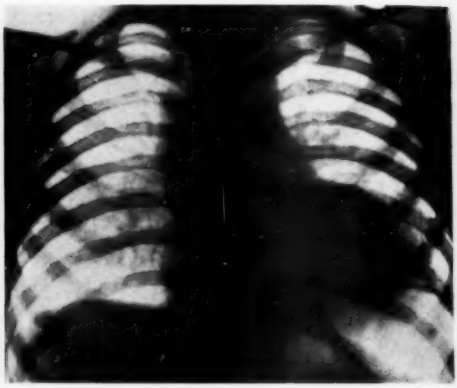

Fig. 5

Figs. 4 and 5. Cases 3 and 4. P.a.-projection, enlargement of the heart to the left corresponding to increased stroke volume in left ventricle.

Gross regurgitation of the contrast medium from the region of the dilated non-coronary cusp was observed, probably because of some incompetence of the cusp.

Case 5. C. L. 1032. This case, which was reported in detail by FALHOLT & THOMSEN in 1953 is mentioned for the purpose of comparison with the cases recorded above. It presents as an example of a congenital aortic sinus aneurysm which had not ruptured and therefore caused no disturbance of the normal haemodynamic conditions. In consequence no enlargement and no abnormality in the shape of the heart could be seen (Fig. 10).

Discussion

The literature contains several papers on the roentgenologic findings in acquired aneurysms of the sinuses of the aorta. LIAN, MARCHAL & DEPARIS 1933 and ÖSTRUM, ROBINSON, NICHOLS & WIDMANN 1938 described the picture observed in acquired aneurysms developed from different parts of the aortic sinuses. Such aneurysms may be caused by syphilitic aortitis, arteriosclerosis, or bacterial endocarditis. Aneurysms, however, in which these causes can be excluded, are generally regarded as congenital aneurysms, *i. e.* aneurysms which develop during life on the basis of an embryologic defect of the tissues forming the root of the aorta.

Reports on congenital aneurysms are much smaller in number than reports on the acquired forms, and reproduction of the roentgen findings in congenital aneurysms have been found only in relation to a few case reports: KING 1942, FOWLER & BEWIL 1951, FALHOLT & THOMSEN 1953 (identical with our Case 5) and FELDMAN, FRIEDLANDER, DILLON & WALLYN 1956. Description and discussion of the roentgen findings

Fig. 6

Fig. 7

Figs. 6 and 7. Thoracic aortography in Case 3. A.p. and left lateral. Abnormal position of ascending aorta, and pouch projecting downwards from dilated right coronary sinus. Retrograde filling of left ventricle due either to rupture of aneurysmal sac or complicating valvular incompetence.

in congenital sinus aneurysms are found in the reports of HIRSCHBOECK 1942, MAYNARD & THOMPSON 1948, JONES & LANGLEY 1949, VENNING 1951, and HEIM de BALSAC 1954.

As already pointed out by JONES & LANGLEY in 1949 on the basis of a study of autopsy reports, there are certain morphological differences between congenital and acquired aneurysms, which are of great diagnostic importance.

Congenital aneurysms are generally less than 4 cm in diameter, while acquired aneurysms will as a rule reach greater proportions.

The situation of congenital aneurysms is most often in the right coronary sinus or the non-coronary sinus. In acquired aneurysms the right coronary sinus is affected slightly more frequently than the other sinuses.

The manner of propagation and rupture of the aneurysm is most often downwards into the chambers of the heart if the aneurysm is a congenital one, while propagation upwards and rupture outside the heart is more likely in acquired aneurysms.

Fig. 8

Fig. 9

Figs. 8 and 9. Thoracic aortography in Case 4. A.p. and left lateral. Enlargement of left coronary and non-coronary sinuses and reflux of contrast medium at level of non-coronary valve.

The small size of congenital aneurysms and the anatomic position of the aortic sinuses inside the heart is in accordance with the fact that the appearance of the heart may be completely normal in the absence of significant disturbances of the normal haemodynamics. The cases of FOWLER & BEVIL 1951 and of FALHOLT & THOMSEN 1953 (our Case 5) illustrate such a condition.

In the presence of abnormal communications following rupture of an aneurysm, roentgen examination of the heart will demonstrate a dilatation of either the left heart alone or of both sides of the heart. In the first case a diagnosis of aortic incompetence is very likely to be made on both physical and roentgenologic examinations and a sinus aneurysm will not generally be diagnosed if a thoracic aortography is not performed. This may probably account for our vain search for recorded cases of congenital aneurysm containing reproductions of roentgen appearances similar to those found in our Cases 3 and 4. The possibility of a congenital aneurysm should always be considered when symptoms of severe aortic incompetence occur in young individuals in whom no signs of syphilitic, arteriosclerotic vascular disease, or bacterial endocarditis can be found.

When bilateral cardiac dilatation is combined with the clinical signs of aortic incompetence, the probability of a sinus aneurysm having ruptured into the right chambers of the heart is high, especially when a rapid increase in the size of the heart shadow occurs after an acute episode with pain in the chest, coughing, and signs of acute heart failure. Roentgen films of cases with similar haemodynamic disturbances, and showing the same characteristic deformation of the heart shadow as demonstrated in our Cases 1 and 2, are found in the reports of KING 1942 and FELDMAN, FRIEDLANDER, DILLON & WALLYN 1956, and a film of similar appearance was described by HIRSCHBOECK 1942 and by ORAM & EAST 1955 (Case 2).

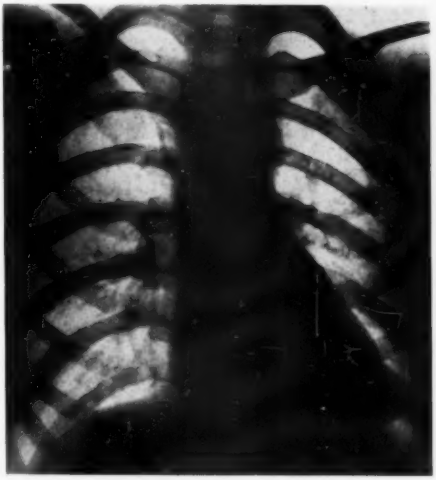

Fig. 10. Case 5. P.a. Normal size and shape of heart corresponding to normal haemodynamics. An aneurysm the size of a walnut was demonstrated in aortograms published previously (FALHOLT and THOMSEN 1953).

Diagnostic procedures. In cases which are clinically suspected of having a congenital aneurysm of the aortic sinuses, special diagnostic procedures are necessary for the detection of those cases in which surgical repair is feasible.

Cardiac catheterization will give information about the presence and size of a shunt into the right heart, and will also reveal the point at which the rupture has extended into the right heart. The diastolic pressure in the right ventricle may indicate the beginning of myocardial failure. Intra-arterial pressure pulse curves and measurement of the systemic blood flow may provide an indirect estimation of the size of the opening into the right heart. Measurement of the pressure in the aorta and the left ventricle may be carried out by means of retrograde arterial catheterization in order to demonstrate stenosis of the aortic valve.

Thoracic aortography is necessary for showing the anatomical relations of the aneurysm and also for direct demonstration of the communication. In anatomic descriptions of the single aortic cusps and sinuses, these are commonly defined by their relation or non-relation to the coronary arteries, and the names right coronary, left coronary and non-coronary sinuses will not cause confusion. For roentgenologic descriptions, however, prefixes such as right, left, anterior, or posterior must be used in cases where

the relationship of the sinuses to the coronary arteries has not been detectable, or in which it might be suspected that the number of sinuses is abnormal. Bicuspid aortic valves have been found in several cases of congenital aortic sinus aneurysm (RICKARDS 1881, HART 1905 (Case 3), GOEHRING 1920, JACOBI & HEINRICH 1933, HIRSCHBOECK 1942, and in our Case 2) and may sometimes cause insufficient valvular function. Demonstration of a bicuspid aortic valve as well as the demonstration of aortic valvular incompetence by thoracic aortography will be difficult unless good filling of all the sinuses with contrast medium is obtained. The injection of the contrast medium must therefore be performed with the tip of the catheter introduced sufficiently deeply into the root of the aorta, *i. e.* about 1 to 1.5 cm above the valves. Control of the localization by registration of the pressure and continuous control of the ECG on a cathode ray oscilloscope may facilitate optimal placing of the catheter without undue risk of occluding the coronaries. From the records quoted above it is seen that bicuspid valves may be formed in different ways, viz. by fusion of the right and left coronary cusps, by fusion of the right coronary and the non-coronary cusp, or by the absence of one of the cusps.

Angiocardiography may be valuable for the determination of the size of the chambers of the heart and the degree of hypertrophy of the ventricular walls.

The electrocardiographic findings have been reported in several of the case reports on congenital aneurysms. Although the findings are in no way constant, there are a few observations, especially when compared with the roentgenologic findings, which may assist the diagnosis.

The low voltage limb leads with no signs of cardiac infarction, found in the case of HIRSCHBOECK 1942, in Case 1 of ORAM & EAST 1955 and in our Case 2, were in contrast to the marked enlargement of the hearts observed on roentgen examination. The haemodynamic conditions in these cases were nearly identical, as all had an aneurysm which had recently ruptured into the chambers of the right heart, as well as an acute dilatation of the heart following the increase in the output of both ventricles.

Electrocardiographic signs of right ventricular hypertrophy have been a constant finding in the unipolar precordial leads from a great number of cases having an atrial septal defect with a marked left-to-right shunt, which has been studied by one of us (DAVIDSEN, unpublished data). No such signs were present, however, in Cases 1 and 2 of the present paper, despite the prominence of a considerable shunt into the right atrium. The absence of electrocardiographic signs of right ventricular hypertrophy is easily understandable in cases where the condition has not existed long enough for the development of hypertrophy such as in our Case 2. In Case 1, however, in which the shunt had been present for more than 7 years, a certain degree of hypertrophy is likely to have developed. An explanation of the absence of electrocardiographic signs of hypertrophy

may possibly be found in the fact that the flow is equally increased in the right and left ventricles whereas, in atrial septal defect, only the right side of the heart is occupied with the transportation of the shunt.

Left axis deviation and signs of left ventricular hypertrophy were found in Cases 3 and 4, in which the haemodynamic pattern was similar to that occurring in aortic incompetence.

General surveys of the electrocardiographic findings in congenital aortic sinus aneurysm have been made by JONES & LANGLEY 1949 and by ORAM & EAST 1955.

Differential diagnosis. After the acquired forms of aortic sinus aneurysms have been excluded there will be certain rare conditions which may make the differential diagnosis difficult. In one patient observed by the authors a typical Valsalva aneurysm with rupture into the right heart was suggested on the basis of the clinical examination. The demonstration of a left-to-right shunt to the right ventricle gave further support to this view. At thoracic aortography, however, a widened coronary artery ending with an aneurysm, which opened into the right ventricle was found (MUNKNER et coll.).

Communication between the left ventricle and the right atrium may exist on account of a rupture of an aneurysm in the membranous part of the ventricular septum. The resulting shunt will affect the output of both ventricles, just as in cases of communication of the aortic sinus aneurysms with the right atrium. The clinical signs, however, will be more similar to those found in ventricular septal defect, and the shunt will not be demonstrable at aortography. It should be remembered that such aneurysms may often be complicated by aneurysm of the aortic sinuses or malformation of the aortic cusps.

Aortico-pulmonary fistulae may cause a murmur which is similar to the findings in aortic sinus aneurysms, but the location of the shunt will be demonstrable both at cardiac catheterization and thoracic aortography.

Pulmonary arterio-venous fistulae or systemic arterio-venous fistulae in the chest wall and aneurysms between bronchial arteries and pulmonary veins may have a murmur of the same character as aortic sinus aneurysms. The diagnosis must be made on angiocardiography or aortography.

SUMMARY

Roentgenologic observations in 5 cases of congenital aneurysm of the aortic sinuses of Valsalva are described. The small size and intracardiac localization of the aneurysms prevents their direct recognition in conventional examinations of the heart. The basis of a clinical diagnosis and the special roentgenologic examinations necessary for the confirmation and differentiation of such diagnosis are considered, and the relationship between the latter examinations and the electrocardiographic findings are discussed.

ZUSAMMENFASSUNG

Röntgenologische Beobachtungen in 5 Fällen mit kongenitalen Aneurysmen des Sinus aortae werden beschrieben. Die Kleinheit und die intrakardiale Lokalisation der Aneurysmen verhindert deren direkte Erkennung bei konventionellen Herzuntersuchungen. Die Voraussetzungen für die Stellung einer klinischen Diagnose und die röntgenologischen Spezialuntersuchungen, die zur Feststellung und Differentiierung einer derartigen Diagnose notwendig sind, werden erwogen und die Beziehungen zwischen den letztgenannten Untersuchungen und den elektrokardiographischen Befunden werden diskutiert.

RÉSUMÉ

Les auteurs décrivent les signes radiologiques dans 5 cas d'anévrisme congénital des sinus de Valsalva de l'aorte. Les petites dimensions et le siège intracardiaque de ces anévrismes empêche de les reconnaître directement sur les radiographies simples du coeur. Les auteurs étudient les bases du diagnostic clinique et les examens radiologiques spéciaux qui sont nécessaires pour le diagnostic positif et différentiel et analysent les corrélations entre les résultats de ces examens et ceux de l'électrocardiogramme.

REFERENCES

Bramwell, C. and King, J. T.: The principles and practice of cardiology, p. 311. Oxford Med. Publications, Oxford 1942.

Davidsen, H. G.: A method of calculation providing directly comparable values for intracardiac shunts in congenital heart disease. Acta med. scand. 158 (1957), 85.

— Fabricius, J. and Husfeldt, E.: Five cases of congenital aneurysm of the aortic sinuses (of Valsalva) and notes on the prognosis. Acta med. scand. 160 (1958), 455.

Falholt, W. and Thomsen, G.: Congenital aneurysm of the right sinus of Valsalva, diagnosed by aortography. Circulation 8 (1953), 549.

Feldman, L., Friedlander, J., Dillon, R. and Wallyn, R.: Aneurysm of right sinus of Valsalva with rupture into the right atrium and into the right ventricle. Amer. Heart J. 51 (1956), 314.

Fowler, E. L. and Bevil, H. H.: Aneurysm of sinus of Valsalva. Pediatrics 8 (1951), 340.

Goehring, C.: Congenital aneurysm of aortic sinus of Valsalva. J. Med. Res. 42 (1920), 49.

Hart, K: Ueber das Aneurysma des rechten Sinus Valsalvae der Aorta und seine Beziehungen zum oberen Ventrikelseptum. Arch. path. Anat. Physiol. 182 (1905), 167.

Heim de Balsac, R.: Anévrysmes congénitaux du sinus de Valsalva. *En:* Donzelot, E., d'Allaines, F., Heim de Balsac, R., Metianu, C., Durand, M. et Dubost, C.: Traité des cardiopathies congénitales, p. 563. Masson, Paris 1954.

Hirschboeck, F. J.: Aneurysm of one of the sinuses of Valsalva caused by a congenital lesion. Case report. Amer. Heart J. 24 (1942), 550.

Husfeldt, E. and Davidsen, H. G.: Surgical treatment of congenital aneurysm of sinus Valsalvae. Acta chir. scand. 111 (1956), 280.

Jacobi, M. and Heinrich, A.: Congenital aorticoventricular fistula with engrafted acute suppurative endocarditis. Amer. J. med. Sci. 186 (1933), 364.

Jones, A. M. and Langley, F. A.: Aortic sinus aneurysms. Brit. Heart J. 11 (1949), 325.

LIAN, C., MARCHAL, M. et DEPARIS, M.: Le diagnostic clinique et radiologique des anévrismes aortiques intrapéricardiques (anévrismes des sinus de Valsalva). Bull. Soc. Méd. Hôp. Paris 49 (1933), 522.

MAYNARD, R. M. and THOMPSON, C. W.: Congenital aneurysm of an aortic sinus. Arch. Path. 45 (1948), 65.

MUNKNER, T., PETERSEN, O. and VESTERDAL, J.: Congenital aneurysm of the coronary artery with an arteriovenous fistula. Acta radiol. (in press).

ORAM, S. and EAST, T.: Rupture of aneurysm of aortic sinus (of Valsalva) into the right side of the heart. Brit. Heart J. 17 (1955), 541.

OSTRUM, H. W., ROBINSON, B. D., NICHOLS, C. F. and WIDMANN, B. P.: Aneurysm of the aortic sinuses or sinus of Valsalva. Amer. J. Roentgenol. 40 (1938), 828.

RICKARDS, E.: Six cardiac and vascular cases: with remarks and engravings. Brit. Med. J. 2 (1881), 71.

SELDINGER, S. I.: Catheter replacement of the needle in percutaneous arteriography. A new technique. Acta radiol. 39 (1953), 368.

THOMSEN, G. and HANSEN, A. T.: Abdominal aortografi. Teknik og diagnostiske erfaringer paa grundlag af 32 tilfælde (Danish). Ugeskr. Læger 116 (1954), 369.

VENNING, G. R.: Aneurysms of the sinuses of Valsalva. Amer. Heart J. 42 (1951), 57.

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ROENTGEN EXAMINATION OF THE SUPRARENAL GLANDS

by

Stig Fagerberg

The roentgen diagnosis of small expansive lesions of the suprarenal glands commonly presents great difficulties. Because the suprarenals cannot be outlined in routine films, much hope has been pinned on the method of *retroperitoneal insufflation of gas*, especially in the form proposed by RUIZ RIVAS (1947). The technique has since been described by several authors, and most recently by COCCHI (1957) in an excellent monograph in which he also gives a comprehensive review of the literature.

Pneumoretroperitoneum or *retroperitoneal pneumography* is technically simple to perform, but assessment of the results is not always easy, since the normal appearance of the suprarenals varies and false conclusions may be drawn from adjacent structures. The following observations and conclusions are based on the findings in a series of over 100 cases examined after the presacral insufflation of 1,000 to 1,500 ml of oxygen. No complications occurred.

Each suprarenal gland is situated between the corresponding kidney and the diaphragm and is enclosed by a fatty capsule within the renal fascia. This capsule, which consists of fat and connective tissue, is intimately connected to the suprarenal gland. The gland and the fatty capsule often appear as a single structure in the pneumogram, since the gas is

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situated between the renal fascia and the capsule. A false picture of the gland, which in obese patients may be incorrectly judged to be enlarged, is thus obtained. This is illustrated by Fig. 1, in which the suprarenal gland appears enlarged, and the normally straight contours of the suprarenal space are convex. At operation, however, a gland of perfectly normal size and shape, surrounded by a large quantity of fat was found.

Fig. 1. Tomogram. Enlarged right suprarenal space. Operation revealed a normal gland surrounded by large quantities of fat and connective tissue.

On the other hand, the suprarenals may be enlarged, even though the suprarenal space appears quite normal if the fatty capsule is normal or underdeveloped. This is illustrated in Fig. 2, in which the left suprarenal gland was judged to be slightly enlarged and the right to be normal. Operation, however, revealed a moderately enlarged right suprarenal and a normal left suprarenal gland.

Exact assessment of the size and shape of the suprarenal gland is thus often impossible by this method and minor variations in the size and outline of the suprarenal space should be judged with caution.

Other sources of error are the normal structures situated close to the suprarenal glands. These include, on the left side, the fornix of the stomach, the tail of the pancreas, and a possible accessory spleen, as pointed out by Cocchi. In the present series a case was misinterpreted as one of right-sided suprarenal neoplasm, but in which, at operation, the right suprarenal was found to be normal. The 'tumour' probably consisted of the partially retroperitoneally situated duodenum surrounded by gas. This assumption is supported by a similar case, in which the duodenum was filled with gas and examined by tomography.

In the present series insufflations were performed in 90 cases of suspected suprarenal disease. The cases are arranged according to the clinical and roentgen findings in Table 1.

Among the 44 cases of hypertension 4 suprarenal neoplasms were discovered in 2 men and 2 women, 3 on the right side and 1 on the left. Both conventional films and urography were normal in 3 of these 4, but retro-

Fig. 2. Tomogram after insufflation of gas. Right suprarenal space appears normal, the left enlarged. Operation showed a normal left gland, the right being slightly enlarged.

peritoneal pneumography revealed neoplasms the size of plums (Fig. 3a). In the fourth case the neoplasm was also evident in the ordinary film. It was larger than a hen's egg, and displaced the kidney downwards and laterally (Fig. 3b). In all four cases the diagnosis of phaeochromocytoma was confirmed at operation.

Of the 41 cases of Cushing's disease, 3 (2 men and 1 woman) were found to have carcinoma of the left suprarenal gland. All three growths were at least the size of a grape-fruit, and could be clearly seen in the conventional films. Retroperitoneal pneumography showed that they lay retroperitoneally (Fig. 4a).

Another woman in this group had slight, irregular enlargement of the left suprarenal. At operation the gland was found to be enlarged 2 to 3 times, weigh 25 g, and the cortex to contain multiple adenomata (Fig. 4b). The diagnostic difficulties are evident on comparing the cases of Figs. 1 and 4b.

Table 1

Clinical diagnosis	Roentgen findings			
	Normal	Tumour	Diffuse enlargement	Total
Hypertension	40	4		44
Cushing's disease	34	3	1+3 ?	41
Adrenogenital syndrome			1	1
Other endocrine disturbances	4			4

a b

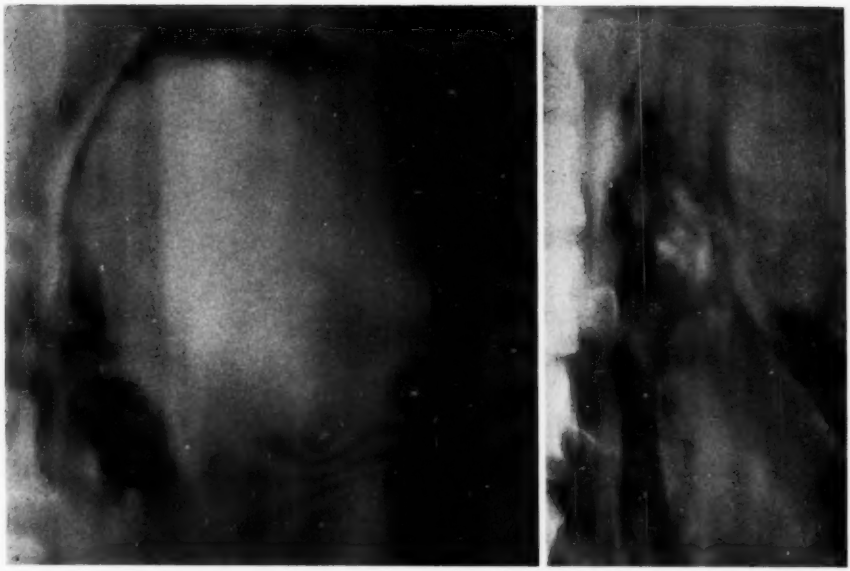
Fig. 3. Tomograms after gas insufflation. a) Left-sided suprarenal tumour. b) Tumour of right suprarenal (arrows). The kidney is displaced downwards and laterally.

In another 3 women in this group one or other suprarenal was thought to be diffusely enlarged (Fig. 2). The correlation between the roentgen and operative findings was poor, however; this is not surprising, since the changes were very small, and the slight enlargement was not accompanied by change in shape of the gland. Pathologic examination revealed hyperplasia of the cortex. The weight of the gland in no case exceeded 15 g (normal: about 10 g).

The case of adrenogenital syndrome in a 5-year-old girl, whose right suprarenal had previously been removed, showed diffuse enlargement of the left suprarenal gland. The patient has not been subjected to further operation.

The findings in all the 4 cases in the group of other endocrine disturbances were judged to be normal, and no operation was undertaken.

The correlation between the roentgen and operative findings in this series is evident from Table 2.



a b

Fig. 4. Tomograms. a) Tumour of left suprarenal. b) Slight enlargement of left suprarenal gland, operatively verified.

Arteriography in cases of neoplasm of the suprarenals is described in the literature (FARIÑAS 1941, NELSON 1942, WEYDE 1952, MILANÉS, MCCOOK and HERNÁNDEZ 1953). The normal vascularization of the glands has been studied by abdominal aortography by JOHNSTONE (1952), MOORE (1952), EVANS (1955), and accounts of aortography combined with retroperitoneal pneumography in suprarenal disease are given by MAY and ROBERT (1953), THOYER-ROZAT et coll. (1954), EVANS (1955), and others.

According to the literature, only large tumours have as a rule been demonstrable where the kidney and renal vessels have been displaced and

Table 2

Operation findings	Cases	Roentgen findings
Phaeochromocytoma	4	+
Carcinoma	3	+
Adenoma	1	+
Hyperplasia	3	— or ?

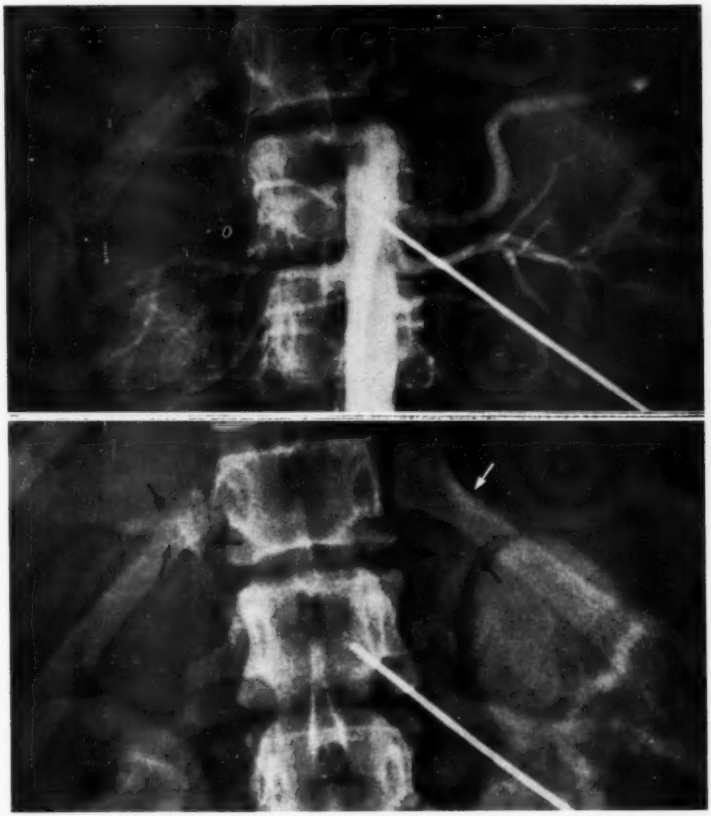


Fig. 5. Abdominal aortography in a case of traumatic cyst of right kidney. *Upper:* Small suprarenal vessels from aorta, clearly visible on right side (arrow). *Lower:* Accumulation of contrast medium in suprarenal tissue (arrows), clearly visible on right side.

considerable pathologic vascularization has been present. In cases in which the changes are only slight, the general opinion seems to be that arteriography is of little or no value.

The suprarenal glands receive their blood supply from three sources, from the aorta, from the renal artery, and from the inferior phrenico-abdominal artery. A study of 50 abdominal aortographies, performed chiefly on renal indications, revealed partial filling of the fine suprarenal vessels in only half of the cases; the origin of these vessels is difficult or impossible to determine since the hepatic and splenic arteries often mask the suprarenal regions (Fig. 6). An accumulation of contrast medium in

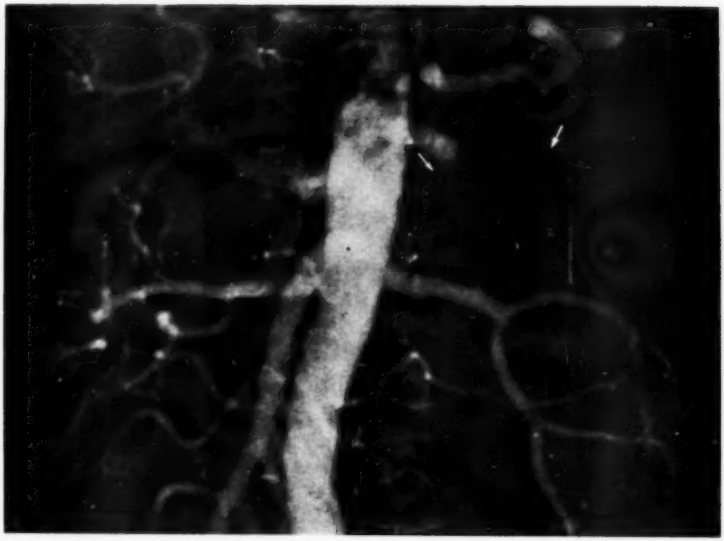


Fig. 6. Abdominal aortography in a case of carcinoma of left suprarenal gland. Renal artery displaced downwards: pathologic vascularization of the tumour (arrows).

the suprarenal tissue could be detected with certainty in only 2 cases (Fig. 5 lower).

Abdominal aortography was carried out by injection directly into the aorta, or by Seldinger's method through a catheter. The exposure rate was 1 to 2 films/second. The normal suprarenal vascularization was usually not assessable by this technique; a higher exposure rate and stereography might possibly be of value. Abdominal aortography was performed in 3 cases of the present series, all with a large carcinoma of the left suprarenal gland. The kidney and renal vessels were greatly displaced, and pathologic vascularization was demonstrable (Fig. 6).

Lesions such as phaeochromocytoma, adenoma, and hyperplasia were not examined by arteriography, and no experience in this field can be reported. The highly vascular phaeochromocytomata, however, should produce rewarding results although there may be risk of hypertonic crises in connexion with the investigation in these cases (AMUNDSEN, AMUNDSEN and MÜLLER 1956). The literature contains no reports on the usefulness of arteriography in the diagnosis of adenoma and hyperplasia, but the often very small changes associated with such conditions would make the procedure seem less promising.

Conclusions

It would seem justifiable to consider retroperitoneal pneumography as the best method available at the present time of demonstrating expansive lesions of the suprarenal glands, although having its limitations. Where the changes are small, the findings should be viewed with caution. An apparently normal suprarenal space may enclose an enlarged suprarenal gland and an apparently slightly enlarged space may be associated with a perfectly normal gland. This state of affairs is explained by the fact that it is not the suprarenal gland itself but the suprarenal space with its contained gland, fat, and connective tissue that is demonstrated by retroperitoneal pneumography. Attempts to determine precisely the size of the suprarenal gland are therefore futile.

SUMMARY

A series of 90 retroperitoneal gas insufflations in cases of suspected suprarenal neoplasms is presented. The difficulties of the roentgen diagnosis of small expansive lesions are stressed; the findings should be viewed with caution. A study of abdominal aortographies carried out on renal indications demonstrate the difficulties of assessing the normal suprarenal vascularization. Aortography was performed with good results in a few cases of large tumours of the suprarenals. The examination was not carried out in any cases of small expansive lesions.

ZUSAMMENFASSUNG

Neunzig retroperitoneale Gaseinblasungen bei Fällen mit Verdacht auf suprarenale Neubildungen werden beschrieben. Die Schwierigkeit, kleine expansive Veränderungen röntgenologisch zu diagnostizieren, wird betont. Die Befunde sollten mit Vorsicht betrachtet werden. Ein Studium abdominaler Aortographien, welche auf Grund renaler Indikationen ausgeführt wurden, zeigt die Schwierigkeiten auf, die sich bei der Beurteilung der normalen suprarenalen Vaskularisierung bieten. Aortographien wurden mit gutem Erfolg in wenigen Fällen mit grossen Tumoren der Nebennieren durchgeführt; die Untersuchung ist aber in keinen Fällen mit kleinen expansiven Veränderungen durchgeführt worden.

RÉSUMÉ

L'auteur présente une série de 90 insufflations rétropéritonéales de gaz dans des cas où on soupçonnait une tumeur surrénale. Il insiste sur les difficultés du diagnostic radiologique des petites tumeurs; les résultats de l'examen doivent être interprétés prudemment. L'étude d'aortographies abdominales faites pour examiner les reins montre combien il est difficile de définir la vascularisation normale des surrénales. L'aortographie a été pratiquée avec de bons résultats dans quelques cas de volumineuses tumeurs des surrénales, mais n'a été faite dans aucun cas de petite tumeur.

REFERENCES

Amundsen, A., Amundsen, P. and Müller, O.: Blood pressure and heart rate during angiocardiography, abdominal aortography, and arteriography of the lower extremities. Acta radiol. 45 (1956), 452.

Cocchi, U.: Retropneumoperitoneum und pneumomediastinum. Thieme Verlag, Stuttgart 1957.

Evans, A.: Combined use of contrast media in retroperitoneal tumours. Arch. Surg. 70 (1955), 191.

Fariñas, P.: A new technique for arteriographic examination of the abdominal aorta and its branches. Amer. J. Roentgenol. 46 (1941), 641.

Johnstone, A.: The visualization of the abdominal aorta and its branches. J. Fac. Radiol. (Lond.) 3—4 (1951/53), 231.

May, J. et Robert, F.: Association de l'aortographie et du pneumorétropéritoine. J. Radiol. Électrol. 34 (1953), 540.

Milanés, B., McCook, J. and Hernández, L.: Aortography and tumors of the liver. Angiology 4 (1953), 312.

Moore, H.: The visualization of the abdominal aorta and its branches. J. Fac. Radiol. (Lond.) 3—4 (1951/53), 240.

Nelson, O.: Arteriography of abdominal organs by aortic injection. Surg. Gynec. Obstet. 74 (1942), 655.

Ruiz Rivas, M.: Nueva técnica de diagnóstico radiográfico aplicado a órganos y estructuras retroperitoneales. Rev. clin. ésp. 25 (1947), 106.

Thoyer-Rozat, P., Reboul, H., Helie, J. et Vergoz, L.: A propos de la valeur actuelle du pneumorétropéritoine et de l'aortographie dans l'étude des glandes surrénales et de la topographie des reins. Presse méd. 62 (1954), 254.

Weyde, R.: Abdominal aortografi, specielt ved nyresykdommer. (Norwegian.) Nord. Med. 47 (1952), 212.

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RÖNTGENOLOGISCHER NACHWEIS PORTO-VENÖSER UND INTERVENÖSER NEBEN-SCHLÜSSE IN DER LEBER

von

H. R. Ney

Das Vorkommen direkter Gefässverbindungen zwischen Arterien und Venen unter Umgehung des Kapillarnetzes ist seit ihrem erstmals gelungenen Nachweis im Müllerschen Körper in den verschiedensten Organen des menschlichen Körpers einschliesslich der Körperoberfläche anatomisch gesichert. Trotz mancher Unterschiede in ihrem anatomischen Aufbau ist diesen Kurzschlüssen die grosse regulatorische Bedeutung für den Gesamtkreislauf und die Eigenversorgung der Organe gemeinsam. Besonders differenzierte und daher schwer zu überblickende Verbindungen sind zu erwarten in Organen, die neben ihrer arteriellen Versorgung zusätzlich ein mehr oder weniger sauerstoffarmes Blutangebot funktionell verwerten und durch einen gemeinsamen venösen Abfluss abgeben. Während sich bei der Lunge bereits eine gewisse Klärung abzuzeichnen beginnt, scheinen die Leberverhältnisse trotz der beträchtlich erweiterten klinischen Kenntnisse noch wenig übersichtlich.

Die anatomische Existenz arterio-portaler Anastomosen scheint allgemein anerkannt zu sein (CLARA). Verbindungen zwischen der A. hepatica und den Lebervenen sind bei verschiedenen Säugetieren ebenfalls beschrieben (ANDREWS, HECKER, MAEGRAITH und RITCHIE).

Bei der Redaktion am 10. Mai 1957 eingegangen.

Bislang herrschte die Ansicht vor, dass porto-venöse Kurzschlüsse ganz im Gegensatz zur Zirrhoseleber bei der gesunden Leber kaum vorhanden sind (ELIAS, HOLLE). Erstmals von BRISSAUD und SABOURIN beschrieben, fanden PRINZMETAL, ORNITZ, SIMKIN und BERGMAN Anastomosen zwischen portalen und hepatischen Venolen. Eigene Untersuchungen machen es jedoch wahrscheinlich, dass diese Verbindungen unter klinischen Verhältnissen in weit grösserer Ausdehnung und Stärke nachweisbar sind, als man bisher angenommen hatte.

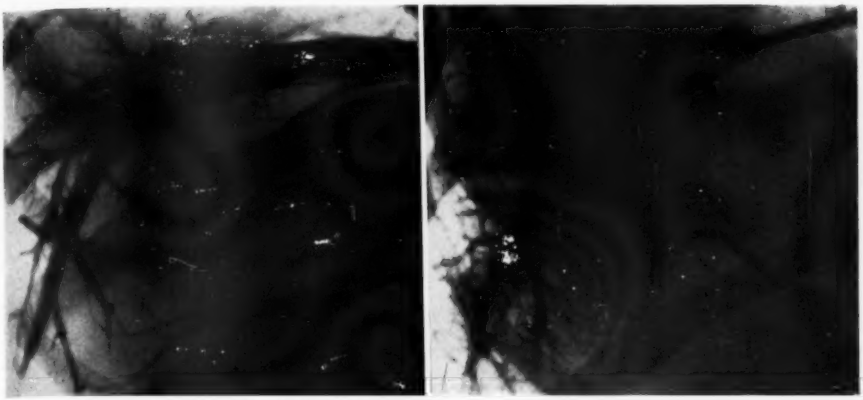
Eigene Untersuchungen

Die Spitze eines Cournand-Katheters wurde in eine Lebervene eingeführt. Am besten eignet sich der rechte Lebervenenhauptast, da seine Lage am besten zu kontrollieren und röntgenologisch am klarsten darstellbar ist. Durch rasche Injektion von 15 bis 18 ccm 70%igem Joduron (CILAG, Alsbach/Bergstrasse, Deutschland) gegen die Blutsäule gelang es, den betreffenden Lebervenenast kontrastreich darzustellen. Zur Bilddarstellung bedient man sich am besten der Serienaufnahmen. Diese bieten auch den Vorteil, die Strömungsrichtung der Kontrastsäulen verfolgen zu können. Bei der hier gezeigten Auswahl des Untersuchungsgutes handelt es sich um eine lebergesunde Frau (Abb. 1) und eine mit Stauungsleber ohne Leberzirrhose (Abb. 2). Die Venographien wurden reaktionslos vertragen.

Auf den Röntgenbildern ist der Lebervenenhauptast bis zu den feindargestellten sublobularen Venen zu sehen (Abb. 1a). Werden durch zu hohen Injektionsdruck die sublobularen Venen überspritzt, erhält man Kontrastfüllung unscharf abgegrenzter Partien des Leberparenchyms. Durch Übertritt des Kontrastmittels durch die Sinusoide (Abb. 1b) oder durch Nebenschlüsse (Abb. 1a) werden neue Gefässgebiete erschlossen, die vom dargestellten Gefässgebiet wegführen, sich aber über die kontrastgefüllten Lebervenenbezirke entleeren. Auch kann das Kontrastmittel, ohne die Sinusoide zu erreichen, durch feine Gefässverbindungen über benachbarte Lebervenen abfliessen, die nicht zum aufgesuchten Leberausflussgebiet gehören (Abb. 2).

Besprechung

Die Angiogramme in Abb. 1 stammen trotz ihrer Verschiedenheit vom selben Patienten. Zweifellos ist die Injektionsrichtung gegen die Leberausflussbahn unphysiologisch, hinzukommt das hochprozentige Kontrastmittel. Das unter hohem Injektionsdruck ausgestossene Kontrastmittel bringt die entgegenströmende Blutsäule für die kurze Dauer der



a b

Abb. 1. Darstellung des rechten Lebervenenhauptastes in einer lebergesunden Patientin. Übertritt des Kontrastmittels in das Pfortadersystem: a) durch porto-venöse Nebenschlüsse, b) auch durch Sinusoide.

Einspritzung ins Stocken. Gestaut und mit Kontrastmittel vermischt, benutzt sie Ausweichmöglichkeiten über angrenzende Niederdruckgebiete mit oder gegen die langsame Strömungsrichtung.

Schon RAPPAPORT, TORI, SERVELLO und DALLA PALMA erwähnen bei ihren Venogrammen den Übertritt des Kontrastmittels in andere Gefässgebiete, ohne aber Untersuchungen über die Art und Weise des Übergangs zu machen. Verfasser ist in einer früheren Darstellung bei der Beschreibung der Kontrastdarstellung der Lebervenen durch den Herzkatheter näher auf diese Erscheinung eingegangen.

Am naheliegendsten ist die Möglichkeit querer Verbindungen der Lebervenen zu ebenfalls abführenden Blutwegen benachbarter Bezirke. In den intervenösen Anastomosen können Bahnen eröffnet werden, die den unphysiologischen Überdruck der dargestellten Lebervenenäste in angrenzende Venengebiete ableiten. Der Übertritt geschieht in Abb. 2 durch kleinkalibrige Kanäle; die allgemeine Verlaufsrichtung der Gefässe ist mit zunehmender Kaliberweite fast parallel mit dem aufgesuchten Lebervenenstamm. Der Beweis, dass sich das Kontrastmittel in andere Teile der Leberausflussbahn entleert, wird geführt durch die Füllung der Einmündungsstelle der Lebervene in die untere Hohlvene. Dass intervenöse Verbindungen vornehmlich bei Stauungsleber vorkommen, liegt unter dem Einfluss der gestaltenden Kraft der Lebervenen (ELIAS) durchaus im Bereich des Möglichen.

Abb. 2. Füllung benachbarter Lebervenengebiete durch intervenöse Gefässverbindungen bei einer Stauungsleber.

Demgegenüber werden in Abb. 1a von den Endaufzweigungen des kontrastgefüllten rechten Lebervenenhauptastes aus über feine Verbindungen Bezirke dargestellt, die nicht zu ihrem Quellgebiet gehören. Ihr Kaliber wird vom dünnen, girlandenförmigen Mittelstück weg nach beiden Seiten hin weiter. Der Verlauf weist ganz im Gegensatz zu Abb. 2 von der Lebervene weg gegen die Pfortaderwurzel zu. Die Ausweichkanäle sind also ganz andere, führen aber wiederum in Niederdruckgebiete der Pfortader, wo ein Druck herrscht, der unter normalen Ruhebedingungen beim gesunden Menschen nur um wenige mm Hg über dem Lebervenendruck liegt (Myers u. Taylor, Berman u. Hull). Der stossartige, plötzliche Überdruck im kontrastgefüllten abführenden Lebervenengebiet mit einem Pressstrahl gegen den Blutstrom ist so hoch, dass die Blut-Kontrastsäule in das Pfortadersystem zurückgedrängt wird. Nach Injektionsschluss entleert sich die gestaute Blutsäule sofort über dieselben Wege zurück in die Lebervene. Es kann sich hier mit grösster Sicherheit nur um porto-venöse Anastomosen (Brissaud u. Sabourin, Prinzmetal, Ornitz, Simkin und Bergman) handeln, die unter Umgehung der Sinusoide die Endaufzweigungen des Pfortadersystems mit dem Lebervenensystem verbinden.

Der andere normale Weg zur Pfortaderseite der Leber geht über das Kapillargebiet, die sog. Sinusoide. In Abb. 1b werden die Sinusoide teilweise erreicht, daneben ist im Angiogramm des gleichen Patienten wie in Abb. 1 a derselbe Hauptast der Lebervene gefüllt, aber bereits die sublobularen Venen sind in weit grösserer Zahl dargestellt. Eigenartigerweise zeigen sich die in Abb. 1a gefundenen Wege zu Pfortaderästen diesmal nicht, dafür formen sich aus den sublobularen und sinusoidalen Lebergebieten mehrere feine Gefässe zu einem grösseren Stamm. Auch dieser hat die Neigung vom Venengebiet wegzuführen und verliert sich schliesslich gegen den Leberhilus zu.

Offen bleibt trotz der erweiterten Kenntnisse des Leberkreislaufes die

Frage der wechselnden Gefässfüllung. Ausser den oben erwähnten technischen Ursachen wird man an die augenblickliche Funktionslage der Leber und die unphysiologische Darstellungsweise ihrer Ausflussbahn durch Injektion gegen die Stromrichtung denken müssen. Wenn schon bei Portogrammen unter Beibehaltung der physiologischen Strömungsrichtung eine völlig unterschiedliche Blutverteilung innerhalb der Leber zutage treten kann (DANIEL u. PRICHARD), wird man bei einem Venogramm, mit hoher Injektionsgeschwindigkeit gegen die Abflussrichtung injiziert, verstärkt mit ähnlichen Reaktionen rechnen müssen. Die auf nervale und humorale Veränderungen rasch reagierende intrahepatische Haemodynamik erfährt zweifellos eine erhebliche Irritation durch den momentanen erheblichen Überdruck. Nur mechanische oder hydrostatische Erklärungsversuche reichen nicht aus zur Analyse dieser eigenartigen Angiogramme. Dafür sprechen auch eigene vergebliche Versuche, am Leichenpräparat zu ähnlichen Gefässdarstellungen zu gelangen.

ZUSAMMENFASSUNG

Durch Katheterisierung einer Lebervene werden retrograde Venogramme der Leberausflussbahn angefertigt. Dabei gelingt der Nachweis von porto-venösen und intervenösen Kurzschlussverbindungen innerhalb der Leber.

SUMMARY

Retrograde venography of the efferent blood flow from the liver was performed by the catheterization of the portal vein. By this means the porto-venous and intervenous anastomoses within the liver were demonstrated.

RÉSUMÉ

L'auteur a pratiqué par cathétérisation de la veine porte une phlébographie rétrograde du courant sanguin efférent provenant du foie. Il a ainsi mis en évidence les anastomoses porto-caves et interveineuses intra-hépatiques.

LITERATUR

ANDREWS, W. H., HECKER, R., MAEGRAITH, B. G. and RITCHIE, H. D.: On direct connections between hepatic artery and hepatic veins in the canine liver. J. Physiol. 122 (1953), 1.

BERMAN, J. K. and HULL, J. E.: Circulation in the normal and cirrhotic liver. Ann. Surg. 137 (1953), 424.

BRAUS, H.: Die Anatomie des Menschen. Bd. II. Springer Verlag, Stuttgart 1934.

Brissaud, E. et Sabourin, C.: Sur la constitution lobulaire du foie et les voies de la circulation sanguine intrahépatique. C. R. Soc. Biol. 40 (1888), 757.
Clara, M.: Die arterio-venösen Anastomosen. Springer Verlag, Wien 1956.
Daniel, P. M. and Prichard, M. M. L.: Variations in the circulation of the portal venous blood within the liver. J. Physiol. 114 (1951), 521.
Elias, H.: A re-examination of the structure of the mammalian liver. Amer. J. Anat. 85 (1949), 379.
Holle, G.: Die gegenwärtige Vorstellung über die gestaltliche und funktionelle Organisation der Leber. Acta hepatol. 3 (1955), 3.
Mann, J. D., Wakim, K. G. and Baggenstoss, P. H.: The vascularisation of the liver. A study by the injections-cast method. Proc. Mayo Clin. 28 (1953), 227.
Myers, J. and Taylor, W.: Occlusive hepatic venous catheterization in the study of portal hypertension. J. clin. Invest. 30 (1951), 622.
Ney, H. R.: Der Bromthaleintest im peripheren und im Lebervenenblut. Klin. Wschr. 35 (1957), 180.
— Die Kontrastdarstellung der Lebervenen im Röntgenbild. Fortschr. Röntgenstr. 86 (1957), 302.
— Die Sauerstoffverhältnisse im Lebervenenblut. Klin. Wschr. 35 (1957), 915.
Prinzmetal, M., Ornitz, E. M., Simkin, B. and Bergman, H. C.: Arteriovenous anastomoses in liver, spleen and lungs. Amer. J. Physiol. 152 (1948), 48.
Rappaport, A. M.: Hepatic venography. Acta radiol. 36 (1951), 165.
Servello, M. et Dalla Palma, L.: La phlébographie hépatique. Presse méd. 62 (1953), 814.
Tori, G.: Hepatic venography in man. Acta radiol. 39 (1953), 89.

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A STUDY OF DOSE LEVELS IN RADIO-IRIDIUM GAMMA-RAY THERAPY

by

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A γ-ray therapy apparatus, using a source of radio-iridium, ^{192}Ir, has been in routine use in the Radiotherapeutic Centre since May, 1950. The first unit of this type, containing about 20 curies and with lead shielding, was introduced by FREUNDLICH, HAYBITTLE and QUICK (1950). This apparatus was succeeded by a unit of improved design containing about 75 curies of ^{192}Ir with uranium metal shielding (FREUNDLICH and HAYBITTLE 1953). Examples of the techniques used and the number of patients with different types of tumours treated by means of these units have been given by MITCHELL (1951, 1955, 1956).

This apparatus was introduced because of the difficulties of obtaining ^{60}Co some years ago, and, in addition to its temporary practical value, has been used to investigate the design and clinical use of short and intermediate distance γ-ray therapy units employing isotopic sources of medium energy. The mean energy of the primary radiation of ^{192}Ir is approximately 0.38 MeV on the basis of half-value layer measurements. With the improved unit, the maximum dose rate is about 28 r per minute at source-skin distance (S. S. D.) 9 cm, and 14 r per minute at 13 cm; larger source-skin distances have been used with correspondingly lower

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dose rates. Both units have been used in much the same way as standard radium teletherapy apparatus. A point of practical importance is that in our experience the radio-iridium unit can replace the use of radium moulds in the treatment of many cases of carcinoma, in sites adjacent to or involving bone and cartilage, *e. g.* pinna, nose and dorsum of hand. This use is time-saving for both patients and staff.

The aim of this study is to evaluate the dose levels to be used in radical radiotherapy with the γ-rays of radio-iridium, ^{192}Ir, under standard conditions of field size, fractionation and overall time. The empirical dose levels selected were based on clinical observation of the tissue reactions in conjunction with previous clinical experience and deductions from earlier studies with radium (MITCHELL 1940). An attempt is made to obtain corrected values of the dose levels by the use of estimates of the late results, both for cure rates and for high dose effects.

In the first part of this paper a comparison is made of the dose levels and clinical results in the treatment of squamous carcinoma of the skin by means of the radio-iridium γ-ray therapy units, the usual filtered 220 to 230 kV roentgen-rays at intensities between 30 and 120 r per minute, and radium moulds. In the second part, the results of treatment of a series of cases of carcinoma of the larynx and pharynx by means of radio-iridium γ-rays and of filtered 220 kV roentgen-rays, delivered at about 35 r per minute, are analysed mainly in connection with the problem of dose levels.

This study is not primarily concerned with the results of treatment. It suffers from the disadvantage of being a retrospective survey. However, the conclusions may be of interest in relation to the design and planning of clinical trials of γ-ray therapy units, especially perhaps those employing ^{137}Cs as source.

I. Treatment of squamous carcinoma of the skin

Selection of cases

This series includes all histologically proved cases of squamous carcinoma of the skin treated between 1st January 1947 and 31st December 1954 by means of either radio-iridium γ-ray therapy, filtered 220 to 230 kV peak roentgen-rays of HVL 0.5 to 2.5 mm copper or external radium moulds, using an overall treatment time of eight days. Cases where histology was not available or uncertain and cases treated in a different overall time or by a lower quality radiation are not included. The γ-ray and the roentgen-ray treatments were almost invariably delivered in 7 fractions while the radium moulds were applied for times between 5 and 8 hours each day.

Table 1

2-year results of treatment of squamous carcinoma of the skin

Radiation	Roentgen-rays				Iridium γ-rays				Radium γ-rays			
Mean age (yrs)	68				70				72			
Mean treated area (cm²)	12				14				17			
Mean follow-up (months)	82				46				79			
Site	Hand	Ear	Other sites	All sites	Hand	Ear	Other sites	All sites	Hand	Ear	Other sites	All sites
Numbers treated	4	13	54	71	10	11	6	27	22	9	1	32
Intercurrent deaths	2	2	4	8	2	0	0	2	2	0	1	3
Failures	0	2	6	8	1	1	1	3	1	0	0	1
Necrosis within 2 yrs	0	1	5	6	0	4	0	4	2	0	0	2
Necrosis after 2 yrs	0	1	2	3	0	0	0	0	2	0	0	2
Symptom-free	2	[1]9	44	[1]55	7	10	5	22	19	[1]9	0	[1]28
Net 2-yr symptom-free rate (%)	(100)	(82)	88	87	(88)	(91)	(83)	88	95	(100)	—	97

[1] One more case failed after 2 years.

Table 2

2-year results of treatment of squamous carcinoma of the skin
Areas 5 to 15 cm² inclusive

Radiation	Roentgen-rays	Iridium γ-rays	Radium γ-rays
Numbers treated	43	14	19
Mean age (yrs)	68	69	71
Mean treated area (cm²)	8	8	10
Mean follow-up (in months)	82	43	86
Intercurrent deaths	5	2	2
Failures	4	1	1
Necrosis within 2 yrs	4	3	1
Necrosis after 2 yrs	3	0	2
Symptom-free	[1]34	11	16
Net 2-year symptom-free rate (%)	90 ± 5	92 ± 7	94 ± 5

[1] One more case failed after 2 years.

The aim here is not to present a picture of results of treatment of all cases of carcinoma of the skin but to use the results obtained in a relatively selected group as a basis for the assessment of the dose levels used with different radiation qualities. The mean ages of the patients treated by each of the three methods were almost the same but the treated areas in the roentgen-ray group tended to be lower than in the other two groups (see Table 1). To avoid possible bias due to this difference an analysis has also been made of the results and dose levels for lesions with areas from 5 to 15 cm² inclusive since with this limitation the mean areas in each group were more comparable (see Table 2).

With regard to the site of the lesions all except one of those treated by radium mould and 78 % of those treated by radio-iridium were on the hand or ear while only 24 % of those treated by roentgen-rays were at these sites. This reflects the deliberate treatment policy of using harder radiation where there was a risk of necrosis in cartilage or underlying bone.

Clinical results

As no cases of carcinoma of the skin were treated by radio-iridium teletherapy before October 1950 the average follow-up period in cases treated by radio-iridium was less than in those treated by radium mould and roentgen-rays but all cases have been followed for at least two years. Furthermore there were only two cases in which a recurrence has occurred after 2 years as compared with twelve failures within the two year period. — A similar ratio of failures within and after 2 years has been reported by Magnusson (1935), Strandqvist (1944) and Smithers and Gordon (1955) — We therefore consider that for the comparison of the results in these cases it is reasonable to use the two-year symptom-free rate as an index.

Table 1 presents the complete results as assessed at 31st December 1956, classified according to radiation quality and site of lesion. Table 2 shows the results for lesions with areas from 5 to 15 cm² inclusive. As may be seen, there are no significant differences between the net 2-year symptom-free rates in each group, and results with each technique have been good. The overall incidence of necrosis was about the same in all groups, although it must be noted that all four cases of necrosis due to iridium treatment occurred within two years, and the number in this group may possibly increase with longer follow-up. Fifteen of the necroses were superficial and transitory. Of the remaining two, one was in the iridium group and preceded a recurrence; the second was in a patient treated by roentgen-rays for a lesion of area about 40 cm² in the right temporal region. The necrosis, developing in the treated area, involved bone, and the patient subsequently died of osteomyelitis. In neither of

these cases could the necrosis be attributed to an extra high dose having been given.

It seems fair to conclude that the dose levels used have been clinically equivalent, with the reservation that if the incidence of necrosis in the iridium group increases with longer follow-up, we should suspect that the dose level in this group had been a little higher than the optimum.

Dose levels

The standard prescription for the roentgen-ray treatments was a minimum tumour dose of 3,500 r, estimated usually at 0.5 to 1 cm depth from the surface of the lesion, depending on its extent. When iridium γ-ray therapy was begun in 1950, it was assumed as a working hypothesis that 1.2 r of iridium γ-rays would produce the same biological effect as 1 r of roentgen rays. The prescribed minimum tumour dose was therefore 4,200 r in 8 days. The doses were measured with a Victoreen r-meter and the same calibration factor was used for both iridium γ-rays and roentgen-rays. A Baldwin-Farmer dosemeter calibrated at the National Physical Laboratory in July 1955 showed the extent of the error in the Victoreen calibration owing to previous errors in the N. P. L. standard to be 7 %, *i. e.* our 3,500 r had in fact been 3,750 r. At the same time the dosemeter was calibrated with a known radium source, and its correction factor found to be 1.05, as compared with 1.0 for roentgen-rays of HVL 2.5 mm copper. Assuming that its correction factor was 1.03 for iridium γ-rays, a comparison with our original method of calibration showed that what had been called 4,200 r was in fact 4,620 r. Where we had aimed at a dose ratio of 1.2, we had therefore actually used a ratio of 1.23. In Table 3 and the remainder of this paper all doses are quoted in correct roentgens.

In the roentgen-ray group two cases received a minimum tumour dose greater than the standard dose of 3,750 r while fourteen cases received less. Of these fourteen, only two failed, *i. e.* the cure-rate was virtually the same as in the group as a whole. In some of these cases a lower tumour dose was actually prescribed, in others the prescription was a surface dose of 3,750 r with no estimated tumour depth. We have therefore calculated the dose 0.5 cm deep in these last cases, in order to obtain the mean minimum tumour doses quoted in Table 3.

In the iridium group one case received more than 4,620 r and two received less. Neither of these failed, and the mean minimum tumour dose of the whole group was still 4,620 r as shown in Table 3. It can be seen therefore that the minimum tumour dose delivered by iridium γ-rays was on the average 1.26 times that delivered by roentgen-rays. Consideration of the areas from 5 to 15 cm^2 led to a figure of 1.22.

Table 3

Mean doses used in 8-day treatment of squamous carcinoma of the skin

Radiation		Numbers treated	Minimum tumour dose		Surface dose	
			r	Ratio to roentgen rays	r	Ratio to roentgen rays
Roentgen-rays	5 to 15 cm²	43	3,720	1.00	4,110	1.00
	All areas	71	3,680	1.00	4,060	1.00
Iridium γ-rays	5 to 15 cm²	14	4,550	1.22	5,120	1.25
	All areas	27	4,620	1.26	5,280	1.30
Radium γ-rays	5 to 15 cm²	19	4,960 (4,630*)	1.33 (1.24*)	6,120	1.49
	All areas	32	4,820 (4,580*)	1.31 (1.24*)	6,080	1.50

* Figure derived with minimum tumour doses calculated at a depth of at least 0.5 cm.

The radium mould doses were calculated by the Manchester method, and were usually limited by considerations of skin dose. However, in all cases the dose was also calculated at what was estimated to be the maximum tumour depth at the time of the treatment. The mean minimum tumour doses at this depth and the mean surface doses are shown in Table 3. It will be seen that the minimum tumour dose with the moulds was not very different from that with iridium γ-rays. Furthermore, in nine of the mould cases the minimum tumour dose was estimated at a depth of from 2 to 3 mm, *i. e.* less than 0.5 cm. This may have been unrealistic, and recalculating the minimum tumour doses in these cases at 0.5 cm, the mean minimum tumour dose of the whole group is reduced to below the iridium figure. There would seem therefore to be no evidence for the existence of any difference between the biological effect as measured by tumour cure-rate of 1 r of radium γ-rays and 1 r of iridium γ-rays.

Because of the short source-skin distance the mean skin dose with the moulds was considerably higher than with iridium teletherapy. This is a further factor which leads us now to treat skin lesions over bone or cartilage by iridium teletherapy rather than by a radium mould.

II. Treatment of carcinoma of the larynx and pharynx

Selection of cases

In this section the results are presented of treatment of carcinoma of the larynx and pharynx. Lesions of the tonsil, post-cricoid and naso-pharynx are not included. Since the beginning of September 1950 iridium

Table 4

Patients classified by site and extent of lesion

	Larynx (In all, 44 cases)					Pharynx (In all, 104 cases)	
	Early cord lesions	Other new lesions		Recurrent cases		New lesions	
		Without glands	With glands	Without glands	With glands	Without glands	With glands
Group A	2	9	0	1	2	12	29
Group B	6	7	3	0	0	19	26
Group C	4	6	2	2	0	5	13
Total	12	22	5	3	2	36	68

γ-ray therapy has been used for radical treatment of most lesions that were not too extensive, while more advanced cases where only palliation was possible were treated by conventional deep roentgen-ray therapy. Before September 1950, only 220 kV roentgen-rays of HVL 1.5 mm of copper were used. The cases have therefore been studied in three groups according to the period during which they were treated (or registered if not treated). The periods were: group A, January 1st 1946 to August 31st 1950; group B, September 1st 1950 to December 31st 1953; group C, 1954 and 1955.

The analysis was made as at 31st December 1956 so that groups A, B and C were followed up for periods of at least 6, 3 and 1 years, respectively. All cases, whether treated or untreated, were included, except four cases who were registered with us but then referred for surgery.

Clinical classification

It was felt that with the numbers available, a detailed division of cases according to site and stage was not justifiable as it would result in the numbers of cases in each division being too small to show any significant trends. The cases were therefore classified according to the following relatively simple scheme.

Larynx: 1) Early cord lesions, *i. e.* lesions confined to one true cord, the mobility of which was not affected; 2) New lesions at other sites within the larynx or extending beyond one cord, without and with secondary glands, respectively; 3) Lesions recurrent after previous treatment, without and with secondary glands, respectively.

Pharynx: New lesions, without and with secondary glands, respectively.

The distribution of the patients among the various classifications is shown in Table 4.

Table 5

Three-year results in groups A and B

Site and extent	Group	Number of cases	Not treated	Inter-current deaths	Alive and well	
					Biopsy positive	Not confirmed by biopsy
Larynx						
Early cord lesions	A	2	0	0	1	1
	B	6	0	0	5	1
Other new lesions:						
Without glands	A	9	0	1	2	1
	B	7	1	0	2	0
With glands	A	0	0	—	—	—
	B	3	0	1	0	0
Pharynx						
New lesions:						
Without glands	A	12	1	0	1	0
	B	19	1	2	2	1
With glands	A	29	2	2	1	1
	B	26	3	1	2	1

Age and sex. The age distributions were similar in larynx and pharynx cases with a mean of 64 years. 5 per cent of the larynx and 12 per cent of the pharynx patients were women.

Length of history. It was found that lengths of history were distributed in an approximately log normal manner (WOOD and BOAG 1950), and that there were no significant differences between the log mean histories of cases in each of the groups A, B and C. Among the early cord lesions there were no histories longer than 11 months, but although the log mean history of these cases was 3.1 months as compared with 4.9 months for other larynx cases and 4.5 months for pharynx cases, the differences were not significant. The incidence of secondary glands appeared to be unconnected with the length of history, and the log mean history of all cases with at least a three-year cure was 3.8 months, not significantly lower than the overall log mean of 4.4 months.

Results

In carcinoma of the larynx and pharynx the number of recurrences after three years is small. The three-year survival rate is therefore a reasonable index of success, and the rates for groups A and B are compared in Table 5.

With early cord lesions the results were good in both groups. In group A one patient was alive and well after 6½ years; the other died of intercurrent disease at 10 years. In group B three patients have survived for

Table 6

Fraction cured 'c', calculated by the 'method of maximum likelihood'

Site and group	All cases		Only cases confirmed by biopsy	
	c	Standard error	c	Standard error
Pharynx				
Group A	0.083	0.046	0.050	0.037
Group B + C	0.155	0.065	0.113	0.050
Group A + B + C ...	0.123	0.036	0.082	0.033
Larynx				
Group A + B + C ...	0.441	0.076	0.406	0.080
Group A + B + C (excluding early cord lesions)	0.297	0.088	0.279	0.089

at least 5 years, while one recurred at 44 months and was admitted for laryngectomy at the time of the survey.

In the other cases of carcinoma of the larynx, numbers were small in each group and there was no significant difference between the results in A and B. No cases with glandular involvement or recurrent cases were cured.

In the pharynx cases the survival rates were higher in group B than in group A, but the differences were not statistically significant. It seemed worthwhile to investigate this point further and to make use of the extra information available in group C. The 'method of maximum likelihood' (Boag 1948) was therefore used to calculate the fraction cured, 'c'.

As predicted by Boag, the distribution of survival times of patients dying of cancer was log normal. The log means and standard deviations were not significantly different in groups A and B, or in larynx cases as compared with pharynx. In all the calculations of 'c' we have therefore used a log mean of 0.840 (6.9 months) and a standard deviation of 0.432 derived from all the larynx and pharynx cases in groups A and B. The results of the calculations are given in Table 6. Two values of 'c' are quoted in each group, one being derived from all patients in the group, the second being calculated after excluding any patient alive and well, or dead from intercurrent disease, whose original lesion was unconfirmed by biopsy. Again, although the fraction cured was higher in the group B + C pharynx cases than in group A, the standard errors indicate that the improvement was not statistically significant. It is of interest to note in this connection that even if a real difference existed of the size shown

Table 7

Mean minimum tumour doses adjusted for an overall time of 32 days

(Cases have only been included where the minimum tumour dose was not less than 4,000 r iridium γ-rays or 3,250 r roentgen rays, and the maximum field dimension was not greater than 9 cm.)

Site	220 kV roentgen-rays		Iridium γ-rays		Dose ratio
	Number of cases	Minimum tumour dose	Number of cases	Minimum tumour dose	
Larynx	11	4,860 ± 210	19	5,820 ± 200	$1.20 \pm 0.06_2$
Pharynx	12	3,980 ± 160	24	5,050 ± 120	$1.27 \pm 0.05_6$
				Weighted mean	$1.24 \pm 0.03_5$

by the values of 'c', 292 cases would be required in each group for us to stand a 90 per cent chance of detecting it at the 5 per cent level of significance (BANKIER and BATLEY 1957), and 237 would be required in each group to stand the same chance of detecting it at the 10 per cent level. We must therefore conclude that the thesis that our results have been better since the introduction of the iridium γ-ray therapy unit is neither proved nor disproved. The last three lines of Table 6 show the values of 'c' for all cases of carcinoma of the larynx and pharynx seen between 1946 and 1955 inclusive. The results are comparable with those reported by other centres.

Dose levels

All treatments were subject to clinical control. Thus, although the assumed dose ratio of 1.2 was used as a guide, the final dose levels, reached after an overall time which was usually from three to six weeks, were determined by other factors such as the time of onset and severity of skin and mucosal reactions. There were no marked differences between the reactions caused by roentgen-rays and γ-rays.

In comparing dose levels, account had to be taken of the fact that the iridium unit was used for radical treatments to fields of 9 cm diameter or less, while 220 kV roentgen-rays were used for all cases in group A, and the larger more advanced lesions in groups B and C. A comparison has therefore been made between the doses received by cases having radical treatment to fields with dimensions not larger than 9 cm. All doses were adjusted to an overall time of 32 days using the time-dose relationship of STRANDQVIST (1944), and radical treatments were specified as those in which a minimum tumour dose was given of at least 4,000 r iridium γ-rays or 3,250 r roentgen-rays. With these limitations the mean minimum tumour doses in Table 7 were calculated. Taking the largest field dimen-

Table 8

Patients with high dose effects

Radiation	Site	Tumour dose in r adjusted to an overall time of 32 days		Symptoms
		Maximum	Minimum	
220 kV roentgen-rays	Pharynx	3,900	3,900	Gross oedema
	»	4,880	4,880	Perichondritis
	»	4,900	4,900	Perichondritis
	Larynx	5,820	5,290	Necrosis
	»	6,360	6,060	Gross oedema
Iridium γ-rays	Pharynx	6,080	5,150	Necrosis
	Larynx	7,530	5,550	Infective oedema[1]
	»	7,750	6,350	Necrosis[2]
	»	8,000	6,400	Gross oedema
	»	6,730	6,730	Infective oedema[1]

[1] Responded to penicillin; patient alive and well.
[2] Patient alive and well after sequestration of cartilage.

sion as an indication of the size of the lesion, the mean sizes for the larynx and pharynx cases treated by roentgen-rays were 5.7 cm and 7.5 cm, respectively. The corresponding means for those treated by iridium γ-rays were 5.8 cm and 6.8 cm. It will be seen that the dose ratio used in the treatment of carcinoma of the larynx was not significantly different from that used in the treatment of carcinoma of the pharynx, although the dose levels were lower in the latter group. The mean values of the doses received by the three-year cured cases alone were not significantly different from the values given in Table 7. The mean dose ratio obtained from both larynx and pharynx groups, weighted according to the number of cases in each group, was 1.24 ± 0.035, which may be compared with the value of 1.26 used in the treatment of carcinoma of the skin.

High dose effects

Excluding cases with recurrent carcinoma of the larynx, there were ten patients who, subsequent to treatment, developed symptoms which could possibly be attributed to excessive dosage. Details of these cases are given in Table 8.

Contrary to what had been hoped, the use of a higher quality radiation did not reduce the incidence of high dose effects. There are two points which should be mentioned in considering this result. One is the possible effect of lower energy components in the iridium γ-ray spectrum and the softening of the beam within a scattering medium. Measurements are reported in an accompanying paper (HAYBITTLE) which show this effect

to be small. The second is the higher ratio of maximum to minimum tumour dose that occurred in iridium γ-ray therapy due to the relatively short source-skin distance. This ratio was about 1.2 as compared with about 1.05 for roentgen-ray treatments. SPIERS (1949), taking into account the microscopic nature of bone, calculated that the bone tissue ionization ratio only increases by 65 per cent as the radiation quality is changed from radium γ-rays to 200 to 250 kV roentgen-rays. For cartilage, which is the tissue most liable to radiation injury in treatments of the larynx and pharynx, the ratio would increase by a much smaller percentage. The higher maximum tumour doses used with iridium γ-ray therapy could therefore have offset the improvement that might have been expected from using a higher quality radiation.

Conclusions

The clinical results presented above do not provide any conclusive evidence that in the treatment of carcinoma of the larynx and pharynx, the use of a short-distance γ-ray therapy unit instead of conventional roentgen-ray apparatus leads to a higher cure-rate. In this particular series, the incidence of high dose effects has also been no less using γ-rays, but, as discussed in the previous section, this does not necessarily invalidate the conclusions reached by SPIERS, and WILSON (1950) from considerations of energy absorption in tissues of varying atomic number. It is possible that the full advantage of high energy radiation in this respect may only become apparent when treatment is given by units having depth doses as good as or better than 200 to 250 kV roentgen-ray apparatus.

Our experience in the treatment of carcinomas of the larynx and pharynx as well as of the skin demonstrates that the original hypothesis that 1.2 r of iridium γ-rays is clinically equivalent to 1 r of 220 kV roentgen-rays is substantially correct. Consideration of the dose ratios in Table 8 suggests that the best value is 1.24 and that the correct value is not likely to be greater than 1.31 or less than 1.17, *i. e.* the relative biological efficiency of iridium γ-rays with respect to 220 kV roentgen-rays lies between 0.76 and 0.86.

SUMMARY

The results of treatment of 130 cases of squamous carcinoma of the skin, 44 cases of carcinoma of the larynx, and 104 cases of carcinoma of the pharynx have been studied with a view to assessing the dose levels to be used with radio-iridium, ^{192}Ir, γ-ray therapy. No significant differences have been found between the results obtained by treatment with either radio-iridium γ-rays or 220 kV roentgen-rays, or, in the cases of carcinoma of the skin only, with radium γ-rays.

ZUSAMMENFASSUNG

Die Behandlungsresultate von 130 spinocellulären Hautkrebsen, 44 Larynxkarzinomen und 104 Pharynxkarzinomen sind mit der Absicht studiert worden, die für die Gammastrahlentherapie mit radioaktivem Iridium, Ir^{192}, notwendigen Dosen festzustellen. Keine signifikanten Unterschiede zwischen den erhaltenen Behandlungsresultaten mit Gammastrahlen des Ir^{192} und 220 kV Röntgenstrahlung oder, nur bei Hautkrebsen, den Gammastrahlen des Radiums sind beobachtet worden.

RÉSUMÉ

Les résultats du traitement de 130 cas d'épithélioma pavimenteux de la peau, de 44 cas de cancer du larynx et de 104 cas de cancer du pharynx ont été étudiés en vue de déterminer la dose à utiliser en gammathérapie par le radio-iridium ^{192}Ir. On n'a pas trouvé de différence importante entre les résultats obtenus par la gammathérapie avec le radio-iridium et ceux obtenus par la roentgenthérapie à 220 kV, ou, dans le cas des cancers cutanés uniquement, par les rayons gamma du radium.

REFERENCES

Bankier, J. D. and Batley, F.: Comparative series in evaluation of cancer therapy. Brit. J. Radiol. 30 (1957), 158.

Boag, J. W.: The presentation and analysis of results in radiotherapy. Brit. J. Radiol. 21 (1948), 128, 189.

Freundlich, H. F. and Haybittle, J. L.: An improved iridium-192 teletherapy unit. Acta radiol. 39 (1953), 231.

— and Quick, R. S.: Radio-iridium teletherapy. Acta radiol. 34 (1950), 115.

Haybittle, J. L.: The quality of iridium γ-rays within a scattering medium. Acta radiol. 49 (1958), 246.

Magnusson, A. H. W.: Skin cancer, a clinical study with special reference to radium treatment, pp. 196—199 and 233—234. Acta radiol. Suppl. 22 (1935).

Mitchell, J. S.: Wave-length effect in the reaction of human skin to X- and gamma radiation. Nature 145 (1940), 105.

— Practical aspects of radioactive isotopes in relation to medical treatment. Brit. med. J. 2 (1951), 747.

— Isotopes. *In:* British practice in radiotherapy, p. 97. Butterworths, London 1955.

— Clinical studies of radio-active isotopes in radiotherapy, including their use in gamma-ray therapy units. Souvenir number of the Ind. J. Roentgenol. (1956), 378.

Smithers, D. W. and Gordon, H.: Cancer of the skin. *In:* British practice in radiotherapy, p. 391. Butterworths, London 1955.

Spiers, F. W.: The influence of energy absorption and electron range on dosage in irradiated bone. Brit. J. Radiol. 22 (1949), 521.

Strandqvist, M.: Studien über die kumulative Wirkung der Röntgenstrahlen bei Fraktionierung, pp. 192 and 245. Acta radiol. Suppl. 55 (1944).

Wilson, C. W.: Dosage of high voltage radiation within bone and its possible significance for radiation therapy. Brit. J. Radiol. 23 (1950), 92.

Wood, C. A. P. and Boag, J. W.: Researches on the radiotherapy of oral cancer. Spec. Rep. Ser. Med. Res. Council London, No. 267 (1950).

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THE QUALITY OF IRIDIUM GAMMA-RAYS WITHIN A SCATTERING MEDIUM

by

J. L. Haybittle

As discussed in a previous paper by MITCHELL and HAYBITTLE, the use of iridium γ-rays instead of 220 kV roentgen-rays in the treatment of carcinomas of the skin, larynx and pharynx has not resulted in a reduction in the incidence of high dose effects. Although the mean energy of iridium γ-rays is 0.38 MeV, the spectrum contains γ-rays of energy as low as 0.136 MeV (ROULSTON and PRINGLE). The following measurements were therefore made to see if these softer components plus the presence of scattered radiation could markedly reduce the effective mean energy of the beam by the time it reached the tumour.

Apparatus and results

Two shallow ionization chambers were used for the experiments (see Fig. 1). They were each 1.5 cm in diameter and 0.1 cm deep, but one was made of aluminium and the other of graphite. The ionization rates in the chambers were measured when they were situated at various depths in a Mix D phantom, the two chambers being at equal distances from the central axis of the beam of radiation, and with their planes

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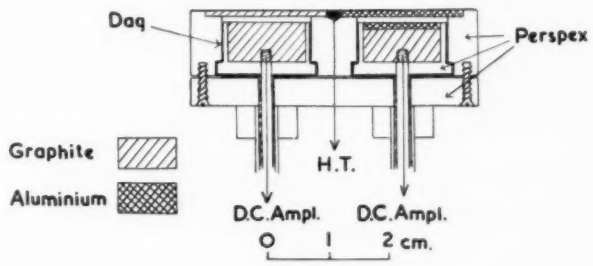

Fig. 1. Ionization chambers.

perpendicular to this axis. At all depths, readings were taken with the positions of the chambers interchanged to allow for any asymmetry in the beam. To find the ratio of the chamber volumes, their front walls were increased to 3 mm thickness and they were exposed to radium γ-rays, when it was assumed that the ionization in the aluminium chamber was 1.1 times that in the graphite chamber (GRAY). The ratios of the ionization/cc in the phantom measurements could therefore be deduced. Diagram 1 shows the results for iridium γ-rays and 220 kV roentgen-rays of HVL 1.5 mm Cu.

Although the atomic number of aluminium is similar to that of bone (SPIERS 1946), that of graphite is lower than that of soft tissue, and the measured ratio will therefore be greater than the ratio of ionization in air cavities surrounded respectively by bone and soft tissue. The dotted

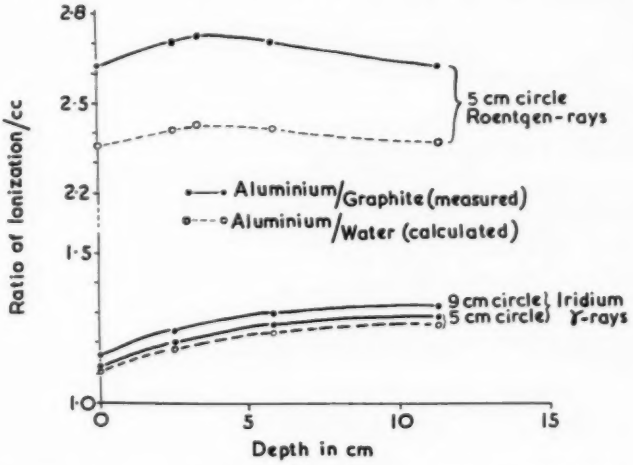

Diagram 1. Ratio of ionization per cc in the two chambers plotted against depth in a wax phantom.

curves in Diagram 1 give the calculated ratio of ionizations in aluminium and water chambers that corresponds to the measured ratio in aluminium and graphite chambers.

Conclusions

The results show that for the small fields used in treating carcinoma of the larynx, the energy absorption in the inorganic matrix of bone is appreciably less with iridium γ-rays than with the roentgen-ray beam, although in some cases the absorption could be about 15 % higher with iridium than with radium γ-rays. In a soft tissue element surrounded by bone, or in cartilage, the difference between iridium and radium γ-rays would be considerably less.

SUMMARY

Measurements with aluminium and graphite chambers have been made to compare the quality of 220 kV iridium γ-rays within a scattering medium with the quality of roentgen rays under the same conditions. The results show that the energy absorption in the inorganic matrix of bone surrounded by soft tissue is appreciably less with iridium γ-rays than with 220 kV roentgen-rays.

ZUSAMMENFASSUNG

Messungen mit Aluminium- und Graphitkammern sind gemacht worden, um die Qualität von Gammastrahlen des Iridiums innerhalb eines streuenden Mediums mit der Qualität von 220 kV Röntgenstrahlen zu vergleichen. Die Ergebnisse zeigen, dass die Energieabsorption in der unorganischen, von Weichteilen umgebenden, Knochenmatrix bei Iridiumgammastrahlen wesentlich geringer ist als bei 220 kV Röntgenstrahlen.

RÉSUMÉ

Des mesures ont été effectuées avec des chambres d'aluminium et de graphite pour comparer la qualité des rayons gamma de l'iridium dans un milieu diffusant avec la qualité des rayons roentgen à 220 kV dans les mêmes conditions. Les résultats montrent que l'absorption d'énergie dans la matrice non organique de l'os entouré de parties molles est notablement moindre avec les rayons gamma de l'iridium qu'avec les rayons roentgen à 220 kV.

REFERENCES

Gray, L. H.: Radiation dosimetry. Brit. J. Radiol. 10 (1937), 721.

Mitchell, J. S. and Haybittle, J. L.: A study of dose levels in radio-iridium γ-ray therapy. Acta radiol. 49 (1958), 233.

Roulston, K. F. and Pringle, R. W.: The decay scheme of ^{192}Ir. Phys. Rev. 87 (1952), 930.

Spiers, F. W.: Effective atomic number and energy absorption in tissues. Brit. J. Radiol. 19 (1946), 52.